UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

In the Matter of **GEMTRONICS, INC.,** **a corporation, and** **WILLIAM H. "BILL" ISELY,** **individually and as the owner of Gemtronics, Inc.**	**DOCKET No. 9330** **Public Document**

COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION

Pursuant to Section 3.24 of the Commission's Rules of Practice, Complaint Counsel moves for summary decision in this matter. Based on the pleadings and other evidence in this case, as described in Complaint Counsel's Statement of Material Facts as to Which There is No Genuine Dispute, Complaint Counsel is entitled to summary decision as to violations of Sections 5(a) and 12 of the Federal Trade Commission Act. The arguments supporting Complaint Counsel's motion are set forth in the accompanying Memorandum in Support of Complaint Counsel's Motion for Summary Decision.

Respectfully Submitted,

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Dated: March 16, 2009

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COMPLAINT COUNSEL'S MEMORANDUM IN SUPPORT OF MOTION FOR SUMMARY DECISION

I. INTRODUCTION

Complaint Counsel moves for Summary Decision, pursuant to Commission Rule of Practice 3.24, against Respondents Gemtronics, Inc. ("Gemtronics"), and William H. Isely ("Isely"), individually and as the owner of Gemtronics. The Federal Trade Commission ("FTC") issued its Complaint in this matter on September 18, 2008, alleging that Respondents violated Sections 5(a) and 12 of the Federal Trade Commission Act ("FTC Act") by making false and unsubstantiated claims that the product, RAAX11, a food or drug within the meaning of Sections 12 and 15 of the FTC Act, is effective in preventing, treating, or curing various types of cancer and that these claims are proven by reliable scientific evidence.

The uncontroverted evidence presented herein reveals that Respondents made false and unsubstantiated cancer claims in Internet advertisements that deceived consumers nationwide about the about the benefits of RAAX11. The evidence presented also clearly demonstrates that scientific evidence does not support any cancer-related claims for RAAX11 and that

Respondents did not possess adequate substantiation for their claims.

Summary decision is appropriate in this case because the evidence demonstrates that Respondents made the alleged claims, in violation of Section 5(a) and 12 of the FTC Act. There is no genuine issue of material fact as to whether Respondents made the representations challenged in the Commission's Complaint, or as to whether such representations are false and unsubstantiated.

Complaint Counsel seeks a proposed order that, among other things, 1) enjoins Respondents from making or assisting others in making false, misleading, or unsupported claims in connection with the marketing of RAAX11 and other health-related products, and 2) requires Respondents to notify their customers who purchased RAAX11 that scientific studies do not demonstrate that RAAX11, or its ingredients, are effective in the treatment of cancer.

II. STATEMENT OF FACTS[1]

A. Respondents' Business

Starting in at least 2004, Respondent Isely was operating a business from his residence that advertised and sold dietary supplements to consumers nationwide through mail order, telephone, and the Internet. (CCSF ¶¶ 3, 4.) He ran this business as a sole proprietor under the assumed name Gemtronics. (CCSF ¶ 3.) In September 2006, Isely incorporated Gemtronics, Inc., a North Carolina corporation, whose principal place of business is located in Franklin, North Carolina, at Isely's residence. (CCSF ¶¶ 1, 4.) Respondent Isely is the owner, registered agent, and general manager of Gemtronics (CCSF ¶ 5.) After incorporating Gemtronics, Isely

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[1] Pursuant to Rule of Practice § 3.24(a), Complaint Counsel has submitted the accompanying Statement of Material Facts As To Which There Is No Genuine Issue ("CCSF") as a separate document.

continued his business advertising and selling dietary supplements through this corporate entity. (CCSF ¶18.)

Since 2004, Respondent Isely and, since 2006, Respondent Gemtronics have advertised and sold the dietary supplement RAAX11 to consumers nationwide through mail order, telephone, and Internet websites, including, *inter alia*, the website www.agaricus.net. (CCSF ¶19.) Since at least 2006, Respondent Isely's name, address and telephone number have been listed in the Internet domain registration for the domain "agaricus.net" as the domain's registrar and its administrative and technical contact. (CCSF ¶ 20.) From 2004 through 2008, Respondents sold approximately 1150 bottles of RAAX11 at a cost of approximately $120 per bottle. (CCSF ¶21.) Respondents charged shipping and handling fees of $15.00. (CCSF ¶ 22)

B. Respondents' Deceptive Advertising Claims for RAAX11

Through the website advertising claims, listed below, found on www.agaricus.net, as well as other claims found elsewhere in the website, Respondents have made both express and implied representations that RAAX11 is effective and/or is scientifically proven to be effective in preventing, treating or curing various types of cancer.

1. Claims that RAAX11 is scientifically proven effective as a treatment or cure of various types of cancer, including but not limited to leukemia, and cancers of the breast, brain, lung, bowel, larynx, and pancreas

Two webpages found on www.agaricus.net contain similar representations that RAAX11 has been proven effective as a treatment or cure of "human cancers," including, but not limited to leukemia, and cancers of the breast, brain, lung, bowel, larynx, and pancreas:

> **Has a cancer killer been discovered?**
> **RAAX11 Extract . . .**

Brazilian scientists have discovered a tropical plant substance that holds great promise in the fight against various types of cancer. . . .

Scientists report that during laboratory tests the substance destroyed cancer cells that had been resistant to treatment up to now. This is a rare occurrence. This substance is so promising it is being kept under wraps at present.
(CCSF ¶ 9.)

Even very resistant Leukemia cells die off

The successful lab tests were carried out on cells from breast- brain- lung- bowel- larynx- and pancreas tumors. "What has been most surprising to us, is the fact that besides these cancer cells, leukemia cells that are normally resistant to a lot of medicines and methods of treatment, were also killed" reported the scientists. It was initially questioned whether the substance, obtained from the Chrysobalanus Icaco plant was suited for the treatment of human cancers, but the results showed that it worked with 90% of the patients.
(CCSF ¶ 7.)

In addition to the representation regarding breast cancer, above, another webpage on the website contains the claim that RAAX11 has been scientifically proven effective in treating or curing breast cancer:

Breast Cancer Patients in remission (2006) 621 out of 749 People in remission taking the RAAX11 protocol

* * *

RAAX11 Offers New Hope for an Alternative Breast Cancer Treatment

In a recent study, 91 women who were suffering from breast cancer at stage IIIb or IV took part in our RAAX11 protocol. By April 2004, 41 women had totally recovered, 23 women were in remission, 27 were stable, and only 9 had not survived, a survival rate of 91.27%.
(CCFS ¶ 9.)

A fourth webpage on www.agaricus.net contains a representation that RAAX11 is effective in treating leukemia:

B-Cell Chronic Lymphocytic Leukemia
Patient, m, 54, in remission taking the RAAX11 protocol.
(CCSF ¶ 9.)

2. Claim that RAAX11 is scientifically proven effective in preventing cancer, including but not limited, to uterine cancer

Beneath the webpage representations, noted above in Section II.B.1., that "scientists have discovered a tropical plant substance" found to be effective in "during laboratory tests," the claim is made in that "ABM" (*agaricus blazei murill* mushrooms), one of the two ingredients in RAAX11, has been proven effective in the prevention of cancer, particularly uterine cancer:

> **Anti cancer effect:** ABM contains natural steroids, known for it's anti cancer effect. . . . It is particularly effective in prevention of uteran cancer.
> (CCSF ¶ 9.)

III. NO SCIENTIFIC EVIDENCE SUPPORTS THE RAAX11 CANCER CLAIMS

In support of its Motion for Summary Decision, Complaint Counsel submits the Expert Report of Dr. Omer Kucuk, an expert in the fields of cancer research and treatment, and in the use of botanical compounds on cancer patients. (CCSF ¶ 23.) Dr. Kucuk is Board Certified in Medical Oncology with the American Board of Internal Medicine. (CCSF ¶ 24.) Dr. Kucuk has been a practicing in the field of medical oncology for over 27 years. (CCSF ¶ 24.) His areas of expertise include cancer prevention, nutrition and cancer, chemoprevention, chemotherapy, medical oncology and clinical trials. (CCSF ¶ 24.) Dr. Kucuk conducts clinical research treating cancers of the prostate, bladder, kidney and testis. (CCSF ¶ 25.) He has authored or co-authored approximately 125 articles published in peer-reviewed scientific journals and more than 20 published book chapters and reviews. (CCSF ¶ 26.)

In his report, Dr. Kucuk states that cancer is not a single disease but many different diseases, and there is no known treatment that is generally accepted as effective for all forms of

cancer. (CCSF¶ 27.) According to Dr. Kucuk, to support cancer treatment claims for a product, qualified experts in the field of oncology would require such claims to be supported by well-conducted, placebo-controlled, randomized, double-blind, clinical trials demonstrating the product's efficacy for the specific type(s) of cancer for which the claims are made. (CCSF¶ 28.)

Dr. Kucuk's report details his review of the RAAX11 product label, the documents submitted by Respondents as substantiation for the RAXX11 product claims, and his own independent search of the existing scientific literature. (CCSF¶ 29.) After completing his review, Dr. Kucuk's expert opinion is that the existing body of scientific literature does not provide competent and reliable evidence that RAAX11, or either of its ingredients *Chrysobalanus icaco ("icaco")* and *Agaricus blazei murill ("agaricus")*, alone or in combination, has been scientifically proven to, or effectively can prevent, treat or cure any form of cancer. (CCSF ¶ 30.)

A. <u>No Scientific Evidence on RAAX11 or Its Ingredients on Cancer Patients</u>

According to his expert report, Dr. Kucuk found no published scientific literature evaluating either RAAX11 or evaluating the combination of *icaco* and *agaricus* as a cancer treatment. (CCSF ¶ 31.) Specifically, Dr. Kucuk reported finding no published scientific literature evaluating the efficacy of RAAX11 or any clinical trial data with RAAX11. (CCSF ¶ 32.) Further, Dr. Kucuk's search of the published scientific literature revealed no articles about the efficacy of taking the combination of *icaco* and *agaricus* as a cancer treatment, or even looking at potential mechanisms of anticancer activity. (CCSF ¶ 33.) In examining the ingredients in RAAX11separately, Dr. Kucuk found no published studies that evaluate *icaco* extract as a cancer treatment nor did he find a single human or animal study of *icaco*. (CCSF ¶ 34.) While Dr. Kucuk's report states that he found eight publications reporting the results of

clinical or human studies using *agaricus,* he found no reports of properly conducted clinical trials regarding the efficacy of *agaricus* extract in patients with cancer. (CCSF ¶ 35.)

Further, specifically evaluating the scientific literature in light of the allegations contained in the Commission's Complaint, Dr. Kucuk concluded that there is no scientific support for the claims that: (1) reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer (Complaint ¶ 6); (2) RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel (Complaint ¶ 8.A.); and (3) RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer (Complaint ¶ 8.B.). (CCSF ¶ 36.)

B. Respondents Provided No Competent and Reliable Evidence to Support the Claims for RAAX11

Respondents submitted three articles downloaded from the Memorial Sloan Kettering database regarding agaricus which were analyzed by Dr. Kucuk in his report. After reviewing the materials, it is Dr. Kucuk's conclusion that the materials do not provide any data from randomized, placebo-controlled clinical trials with cancer patients and therefore, they do not provide any additional relevant clinical data to substantiate or otherwise support the cancer claims challenged in the Commission's Complaint for RAAX11. (CCSF ¶ 50.)

IV. RESPONDENTS HAVE VIOLATED SECTION 5 AND 12 OF THE FTC ACT

A. Respondents' Advertising Claims are Facially Clear and Material

An advertisement is deceptive if it contains a representation or omission of fact that is likely to mislead consumers acting reasonably under the circumstances, and that representation or omission is material to consumers' purchasing decisions. *FTC Policy Statement on*

Deception, 103 F.T.C. 174, 175 (1984) (Deception Statement); *see, e.g., Telebrands Corp.*,140 F.T.C. 279, 290 (2005); *Novartis Corp.*, 127 F.T.C. 580, 679 (1999), *aff'd*, 223 F.3d 783 (D.C. Cir. 2000); *Stouffer Foods Corp.*, 118 F.T.C. 746, 798 (1994); *Kraft, Inc.*, 114 F.T.C. 40, 120 (1991), *aff'd*, 970 F.2d 311 (7th Cir. 1992), *cert. denied*, 507 U.S. 909 (1993). Advertising claims are also presumed to be material if they are express or if they pertain to the purpose, safety, or efficacy of the product. *Deception Statement*, 103 F.T.C. at 182, *see, e.g., Telebrands Corp.*,140 F.T.C. 379, 450 (Initial Decision 2004).

The *prima facia* evidence of what representations an advertisement conveys to reasonable consumers is the advertisement itself. *Deception Statement*, 103 F.T.C. at 176; *see, e.g., Telebrands Corp.*,140 F.T.C. at 290; *Novartis,* 127 F.T.C. at 680; *Stouffer*, 118 F.T.C. at 798; *Kraft*, 114 F.T.C. at 121. When the language of an advertisement is clear enough to permit the Commission to conclude with confidence that the ad can reasonably be read to contain a particular claim, a facial analysis, alone, will permit the Commission to conclude that the ad contains the claim. *Stouffer Foods Corp.,* 188 F.T.C. 746, 798, *citing Kraft, supra,* at 121 and *Thompson Medical Co.*, 104 F.T.C. 648, at 789 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986), *cert. denied,* 479 U.S. 1086 (1987). Thus, where the language in the challenged advertisement is clear, the Commission may rely on the ad itself and need not resort to extrinsic evidence to determine if the claim is conveyed to reasonable consumers. *Novartis*, 127 F.T.C. at 680; *see Stouffer*, 118 F.T.C. at 798; *Deception Statement*, 103 F.T.C. at 176.

Applying this standard, claims made in Respondent's advertisements highlighted are clear on their face. Therefore, there is no requirement for extrinsic evidence to determine if these claims are conveyed to reasonable consumers. In fact, Respondents have not contested that the

claims were made. (Answer ¶ 5.) Respondents' advertising claims are also material, not only because they are express, but also because they relate to the purpose, safety, and/or efficacy of RAAX11, a product advertised specifically as a cancer prevention, treatment and cure. *See, e.g., Deception Statement*, 103 F.T.C. at 182.

B. Respondents' Claims are False and Unsubstantiated

The Commission has consistently held that objective claims made without a reasonable basis constitute a deceptive practice in violation of Section 5. *FTC Policy Statement Regarding Advertising Substantiation*, 104 F.T.C. 839 (1984) (*Substantiation Statement*); *see, e.g., Automotive Breakthrough Sciences, Inc.*, 126 F.T.C. 229, 293 & 293 n.20 (1998); *Jay Norris, Inc.*, 91 F.T.C. 751, 854 (1978), *aff'd as modified*, 598 F.2d 1244 (2d Cir. 1979), *cert. denied*, 444 U.S. 980 (1979). What constitutes a reasonable basis is an objective standard: advertisers must possess at least the level of substantiation expressly or impliedly claimed in the advertisement. *See Honeywell, Inc.*, 126 F.T.C. 202 (1998); *FTC v. Natural Solution, Inc.*, No. CV 06-6112-JFW, 2007 U.S. Dist. LEXIS 60783, at *10 (C.D. Cal. Aug. 7, 2007) (citing *FTC v. U.S. Sales Corp.*, 785 F. Supp. 737, 748 (N.D. Ill. 1992).

For health and safety claims, advertisers must possess competent and reliable scientific evidence substantiating their claims in order to have a reasonable basis for such claims. *See FTC v. National Urological Group, Inc.*, No. 1:04-CV-3294-CAP, 2008 U.S. Dist. LEXIS 44145, at *77 (N.D. Ga. June 4, 2008) (granting FTC's summary judgment motion, court finds safety and efficacy claims for dietary supplements must be substantiated by competent and reliable scientific evidence); *Natural Solution*, 2007 U.S. Dist. LEXIS 60783, at *11-13 (granting FTC's summary judgment motion, court requires competent and reliable scientific evidence for cancer prevention and treatment claims for product); *FTC v. QT, Inc.*, 448 F. Supp.

2d 908, 961 (N.D. Ill. 2006) *aff'd,* 512 F.3d 858 (competent and reliable scientific standard applied for evidence that bracelet relieves pain). Competent and reliable scientific evidence is typically defined as tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results. *See, e.g., Brake Guard Products, Inc.*, 125 F.T.C. 138 (1998); *ABS Tech Sciences, Inc.*, 126 F.T.C. 229 (1998).

To provide adequate substantiation to support the truthfulness of health-related efficacy claims, courts have consistently required double-blind, placebo-controlled studies. *See, e.g., FTC v. SlimAmerica, Inc.*, 77 F. Supp. 2d 1263, 1274 (S.D. Fla. 1999) (double-blind study of the combination of product's ingredients required to support product claims); *FTC v. Sabal,* 32 F. Supp. 2d 1004, 1008-09 (N.D. Ill. 1998) (study found not valid as substantiation, in part, because neither blinded nor placebo controlled); *FTC v. QT, Inc.*, 448 F. Supp. 2d at 962 (medical claims for bracelet required a well-conducted, placebo-controlled, randomized, double-blind study).

The product at issue in this case, RAAX11, is dietary supplement that is advertised and sold as a cancer treatment, prevention and cure. Respondents' advertising representations relate to health and safety and, thus, require substantiation consisting of competent and reliable scientific evidence. As noted above, Complaint Counsel's expert, Dr. Kucuk concludes that to support cancer treatment claims for a product, qualified experts in the field of oncology require randomized, well-controlled, and double-blinded clinical trials demonstrating a product's efficacy for the specific type(s) of cancer for which the claims are made. After examining the substantiation submitted by Respondents, as well as examining the current state of peer-reviewed scientific literature regarding RAAX11 and its ingredients, it is Dr. Kucuk's expert opinion that

there is no competent and reliable scientific evidence that RAAX11 effectively can, or is scientifically proven to, prevent, treat, and cure cancer. Therefore, Respondents lacked a reasonable basis for their advertising claims for RAAX11, and accordingly, have violated Sections 5 and 12 of the FTC Act.

V. RESPONDENTS ARE LIABLE FOR FTC ACT VIOLATIONS

A. Liability of Respondent Gemtronics

The corporate Respondent Gemtronics, by and through its owner, William Isely, violated Sections 5 and 12 of the FTC Act. Gemtronics fulfilled orders for RAAX11 made on the website www.agaricus.net. (CCSF ¶¶ 12-17.) On January 3, 2008, and again on January 28, 2008, an FTC Investigator purchased RAAX11 from the website www.agaricus.net. (CCSF ¶¶ 12-17.) A confirmation webpage from the purchase stated: "Your Credit Card is charged using a SSL secured server. On your statement will appear "GEMTRONICS SECURE PAYMENTS." (CCSF ¶ 15.) The two packages of RAAX11 received by the FTC were sent by Gemtronics and included Gemtronics invoices indicating that payment had been made to the company, one of which stated that Gemtronics was responsible for retail sales. (CCSF ¶¶ 14-17.) The promotional literature in one package included a Gemtronics brochure stating "for more information . . . go to the website www.agaricus.net and click on USA sales" and providing telephone and email contact information for Gemtronics. (CCSF ¶ 17.)

B. Individual Liability of Respondent Isely

The Commission and the courts examine, separately or in combination, a number of factors when determining individual liability: the unlawful practices involved; the respondent's involvement with the practices; the type of corporate entity; the respondent's ownership interest; the corporate office (if any) held; and the influence he exercised over corporate affairs.

Telebrands Corp., 140 F.T.C. at 450; *National Housewares*, 90 F. T. C. 512, 598 (1977).

Gemtronics is a closely-held corporation and Respondent Isely is its owner and manager. (CCSF ¶ 5.) Both the courts and the Commission have held that it is appropriate to hold the owner of a closely-held corporation individually liable because his inclusion in the order would be necessary to make the order fully effective in preventing future violations of the law. *See, e.g., FTC v. Standard Education Society,* 302 U.S. 112, 119-20 (1937) (managers and sole stockholders held liable); *Fred Meyer, Inc. v. FTC*, 359 F.2d 351, 367-68 (9th Cir.), *cert. denied,* 308 U.S. 908 (1967) n.60.

Respondent Isely clearly is liable in this case because he was actively involved in and controlled every facet of Gemtronics' business. Respondent Isely ran Gemtronics business from his home and controlled the company's bank account. (CCSF ¶¶ 3, 6, 38.) Further, Respondent Isely individually participated in the acts and practices at issue in this matter. Isely acknowledged personally fulfilling the two orders for RAAX11 that were placed on the www.agaricus.net website by the FTC. (CCSF ¶ 39.) In addition, Isely was personally identified on the Gemtronics packages, invoices, and in the promotional literature received by the FTC and Isely admitted that these were his materials. (CCSF ¶ 40.)

Respondent Isely also played an integral part in the website www.agaricus.net. As discussed, *supra*, the "agaricus.net" domain was registered in Isely's name. (CCSF ¶ 20.) Respondent Isely admitted that he received notices in the mail for the renewal of the domains that were registered in his name and he produced a renewal notice for "agaricus.net" that had been mailed to him. (CCSF ¶ 41.) In addition, Isely was prominently featured throughout the website

and his name and telephone number were included on a number of webpages on www.agaricus.net as a contact for consumer to purchase RAAX11, to obtain product information, and to participate in an "ongoing study in the USA" of RAAX11. (CCFS ¶¶ 7-11.) In fact, Respondent Isely admitted that when consumers purchase products on the website www.agaricus.net using a credit card, that Isely receives the payment. (CCSF ¶ 42.)

The courts and the Commission have held that, when liability is based on personal participation in the unlawful acts, nothing more need be shown. *See, e.g., Removatron Int'l Corp.*, 111 F.T.C. 206, 290 (1988), *aff'd,* 884 F.2d 1489 (1st Cir. 1989); *FTC v. NCH*, 1995-2 Trade Cas. (CCH) ¶71,114, at 75,351 (D. Nev. Sept. 6,1995).

As shown above, Respondent Isely should be held individually liable because of the type of corporate entity Gemtronics is and because of Respondent Isely's ownership interest in the company. In addition, Respondent Isely had authority to and did control the acts and practices of Respondent Gemtronics. Moreover, he directly participated in the acts and practices at issue in this case. Finally, finding Respondent Isely individually liable is necessary in order to ensure fully effective relief for the deceptive practices alleged in the Commission's Complaint.

Accordingly, given Respondent Isely's creation of and control over the practices of the corporate Respondent Gemtronics, and based upon his personal participation in the website and sales emanating from it, Respondent Isely should be held individually liable for violations of Sections 5 and 12 of the FTC Act.

VI. SUMMARY DECISION STANDARD

Commission Rule of Practice 3.24(a)(2) provides that summary decision "shall be

rendered . . . if the pleadings and any depositions, answers to interrogatories, admissions on file, and affidavits show that there is no genuine issue as to any material fact and that the moving party is entitled to such decision as a matter of law." Rule 3.24(a)(3) provides that once a motion for summary decision is made and adequately supported, "a party opposing the motion may not rest upon the mere allegations or denials of his pleading; his response, by affidavits or as otherwise provided in this rule, must set forth specific facts showing that there is a genuine issue of fact for trial." *See also Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986); *Adikes v. S.H. Kress & Co.*, 398 U.S. 144, 157 (1970). The provisions of FTC Rule 3.24 are virtually identical to the provisions of Fed. R. Civ. P. 56, governing summary judgment in the federal courts. *In re Kroger Co.*, 98 F.T.C. 639, 726 (1981); *Hearst Corp.*, 80 F.T.C. 1011, 1014 (1972).

The Supreme Court has held that where the record, taken as a whole, could not lead a rational trier of fact to find for the non-moving party, there is no genuine issue for trial. *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587 (1986). The party moving for summary judgment must satisfy the evidentiary burden that it would bear at trial. *See Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 254 (1986). If the moving party meets its burden, the opposing party must come forward with specific facts showing there is a genuine issue for trial. *See Matsushita*, 475 U.S. at 585-88. The "mere existence of some alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment." *Liberty Lobby*, 477 U.S. at 247-48.

A determination of whether an advertising practice complies with the laws or regulations enforced by the FTC is a question of law that can be resolved on summary decision. *See FTC v.*

Bronson Partners, 564 F. Supp. 2d 119 (D. Conn. 2008) (granting summary judgment for FTC, court found defendants made deceptive advertising claims for purported weight-loss product); *FTC v. National Urological Group, Inc.*, No.1:04-CV-3294, 2008 U.S. Dist. LEXIS 44145 (N.D.Ga. June 4, 2008) (granting FTC's summary judgment motion, court found defendants deceptively advertised dietary supplements); *FTC v. Natural Solution, Inc.*, No. 06-6112,2007 U.S. Dist. LEXIS 60783 (C.D.Cal. Aug. 7, 2007) (summary judgment ruling that defendants' advertisements for a purported cancer treatment were deceptive).

As set forth above, there is no genuine issue as to any material fact relating to whether Respondents made the representations challenged in the Commission's Complaint. In addition, there is no genuine issue as the fact that Respondents' advertising representations were false and unsubstantiated. Accordingly, Complaint Counsel is entitled to summary decision as a matter of law.

VII. THE PROPOSED ORDER

Complaint Counsel respectfully requests that the Court enter the accompanying proposed Order. The proposed Order is substantially similar in form and content to those recently approved by the Commission in cases challenging deceptive advertising of bogus cancer cures. *See, e.g., FTC v. Westberry Enterprises, Inc.*, 2008 F.T.C. LEXIS 99 (F.T.C. Sept. 18, 2008).

The proposed Order prohibits Respondents from making the types of misrepresentations that gave rise to the violations in this matter. Specifically, Part I of the proposed order would require that Respondents possess and rely upon competent and reliable scientific evidence that

substantiates any representations they make about the ability of the RAAX11, any substantially similar products, and any other covered products (as defined in the order), to prevent, treat or cure cancer. Part II of the proposed order would prohibit Respondents from making representations about the comparative benefits, performance, efficacy, safety or side effects of any covered product or service, unless they have the required substantiation. Part III prohibits any misrepresentations regarding the existence, contents, validity, results, conclusions, or interpretations of any test or study.

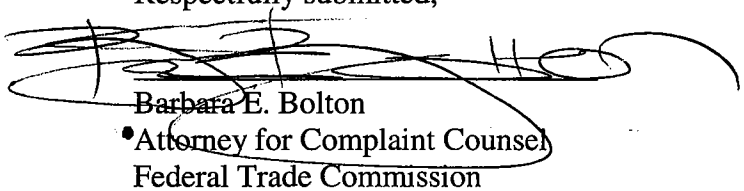
Part IV of the proposed order is the FDA Safe Harbor provision allowing representations permitted in labeling by the FDA. Part V requires Respondents to provide notice via first class mail to consumer purchasers that the product claims for RAAX11 are false or unsubstantiated. The remaining provisions, Parts VI through X of the proposed Order, contain the standard administrative record-keeping and reporting requirements.

VIII. CONCLUSION

For the reasons stated above, Complaint Counsel respectfully request that this motion for summary decision be granted.

Dated: March 16, 2009

Respectfully submitted,



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COMPLAINT COUNSEL'S STATEMENT OF MATERIAL FACTS AS TO WHICH THERE IS NO GENUINE ISSUE

Pursuant to Commission Rule of Practice 3.24, 16 C.F.R. § 3.24, and in support of its motion for summary decision, Complaint Counsel submits this separate statement of material facts as to which there is no genuine issue.

1. Respondent Gemtronics, Inc. ("Gemtronics") is a North Carolina corporation with its principal office or place of business at 964 Walnut Creek Road, Franklin, North Carolina 28734. Respondents' Answer to FTC's Complaint, dated October 10, 2008 (hereinafter "Answer") ¶ 1.

2. Respondent William H. Isely ("Isely") resides at is 964 Walnut Creek, Franklin, North Carolina, 28734. Answer ¶ 2.

3. Beginning in 1993, and continuing thereafter, Respondent Isely owned and operated a sole proprietor business under the unregistered assumed name Gemtronics in which sold dietary supplements from his home via mail order, telephone and the Internet. Respondent William Isely's Answers to Interrogatories, February 3, 2009, (hereinafter "Isely Ints. Resp.") No. 1, 2, 8; Exhibit A to Isely Ints. Resp. (hereinafter "Isely Ints. Resp. Ex. ___."); Isely Deposition Transcript (hereinafter "Isely Dep.") 12-13.

4. Respondent Isely incorporated Gemtronics, Inc. in North Carolina in 2006. Answer ¶ 1; Isely Ints. Resp. No. 2; Isely Dep. 31, 99-100, Respondents' Exhibit to Isley Dep. (hereinafter "Resp. Ex.") 1.

5. Respondent Isely is the owner, registered agent, and general manager of Gemtronics. Isley Ints. Resp. 1; Isely Dep. 101, 105, Resp. Ex. 1; Isely Dep. Complaint Counsel's

Exhibit to Isely Dep. (hereinafter ("CC Ex.") 6.

6. Respondent Isely registered Gemtronics, Inc., located at his home, as an FDA approved warehouse to import dietary supplements for resale. Isely Ints. Resp. No. 13; Isely Dep. 19-21.

7. On December 12, 2007, FTC Investigator Michael S. Liggins ("Liggins") found advertisements for RAAX11 that also included Respondent Isely's name and telephone numbers on the website www.agaricus.net. On that same date, December 12, 2007, Liggins reviewed and preserved to a CD an exact copy of this website. Exhibit B to the Commission's Complaint in this matter is taken from this CD. Complaint Counsel's Summary Decision Exhibit (hereinafter "S.D. Ex. __") 2, Declaration of Michael S. Liggins, FTC Investigator, dated March 12, 2009 (hereinafter "Liggins Dec.") ¶ 6.A., Att. C.

8. On December 13, 2007, Liggins printed out copies of webpages directly from captured CD of the website www.agaricus.net that included RAAX11 and either references to Respondent Isely and/or his telephone numbers. S.D. 2 (Liggins Dec. ¶ 6.B., Att. D.)

9. On January 3, 2008, Liggins found advertisements for RAAX11 that also included the name and telephone numbers for Respondent Isely on the website www.agaricus.net. On that same date, January 3, 2008, Liggins reviewed and preserved to a CD an exact copy of this website. Exhibits A, C, and D to the Commission's Complaint in this matter are taken from this CD. S.D. 2 (Liggins Dec. ¶ 6.C., Att. E.)

10. On January 30, 2008, Liggins printed out copies of webpages directly from the website www.agaricus.net that included RAAX11 and either references to Respondent Isely and/or his telephone number. S.D. 2 (Liggins Dec. ¶ 6.D., Att. F.)

11. At each time that Liggins reviewed the website www.agaricus.net, the only telephone numbers that Liggins found listed on the website for information on, or product ordering for RAXX11 in the United States were those belonging to Respondent Isely. S.D. 2 (Liggins Dec. ¶ 6.E.) (*see also* Liggins Dec. ¶ 4, Att. A. (Verizon CID Response identifying Respondent Isely as the owner of the telephone numbers.))

12. On January 3, 2008, Liggins made an undercover purchase of one bottle of RAAX11 from the Internet website www.agaricus.net. S.D. 2 (Liggins Dec. ¶ 7, Att. I.)

13. On January 17, 2008, Liggins received the package containing the bottle of RAAX11. The package was mailed by U.S. mail from Franklin, NC and listed William Isely, 964 Walnut Creek Road, Franklin, NC 28734 as the sender. S.D. 2 (Liggins Dec. ¶¶ 8, 9, Att. I.)

14. Included in the shipment of RAAX11 ordered by Liggins was an invoice for the purchase from Gemtronics at 964 Walnut Creek Road, Franklin, NC 28734, and included

Respondent Isely's telephone number and email address. The invoice also identified William Isely as the general manager of Gemtronics for retail sales. S.D. 2 (Liggins Dec. ¶ 9, Att. I.)

15. On January 23, 2008, Liggins made a second undercover purchase of one bottle of RAAX11 from the Internet website www.agaricus.net. The Internet confirmation webpage from the website stated: "Your Credit Card is charged using a SSL secured server. On your statement will appear "GEMTRONICS SECURE PAYMENTS." S.D. 2 (Liggins Dec. ¶ 10, Att. J.)

16. On February 11, 2008, Liggins received the package containing the bottle of RAAX11. The package was mailed by U.S. Express Mail from Franklin, NC and listed William Isely and Gemtronics at the Walnut Creek Road as the sender. S.D. 2 (Liggins Dec. ¶¶ 11, 12, Att. J.)

17. Included in the shipment of RAAX11 ordered by Liggins was an invoice for the purchase from Gemtronics and promotional literature for RAAX11. The package invoice was from Gemtronics at 964 Walnut Creek Road, Franklin, NC 28734, and listed Respondent Isely's telephone number and email address as well as a note from him asking that future orders be placed with him directly by phone or email. The promotional literature included in the package from Gemtronics consisted of three printed color pages. One promotional page included the heading "Takesun U.S.A." and directed consumers to go to the website www.agaricus.net and "click on USA sales," and listed Gemtronics and a telephone number and an email address for Respondent Isely to obtain more product information. S.D. 2 (Liggins Dec. ¶ 12, Att. J.)

18. After incorporating Gemtronics, Isely continued his business advertising and selling dietary supplements through this corporate entity. Isely Ints. Resp. No. 13; Isely Dep. 19-21; S.D. 2 (Liggins Dec. ¶¶6 - 12, Atts. C-J.)

19. Since 2004, Respondent Isely and, since 2006, Respondent Gemtronics have advertised and sold the dietary supplement RAAX11 to consumers nationwide through mail order, telephone, and Internet websites, including, *inter alia*, the website www.agaricus.net. Ints. Resp. No. 3; Isely Dep. 34-35, 38, 39-40; S.D. 2 (Liggins Dec. ¶¶6 - 12, Atts. C-J.)

20. Since at least 2006, Respondent Isely's name, address and telephone number have been listed in the Internet domain registration for the domain "agaricus.net" as the domain's registrar and its administrative and technical contact. Isely Ints. Resp. No. 1; S.D. 2 (Liggins Dec. ¶ 5.A.)

21. From 2004 through 2008, Respondents sold approximately 1150 bottles of RAAX11 at a cost of approximately $120 per bottle. Isely Ints. Resp. No. 3; Isely Dep. 41-42.

22. Respondents charged shipping and handling fees of $15.00. S.D. 2 (Liggins Dec. Atts. I, J.)

23. Dr. Omer Kucuk is an expert in the fields of cancer research and treatment, and in the use of botanical compounds on cancer patients. Complaint Counsel's Summary Decision Exhibit 4 is the Expert Report of Dr. Omer Kucuk, ¶¶ 1, 9 (hereinafter cited as Kucuk ¶ ___.)

24. Dr. Kucuk is Board Certified in Medical Oncology with the American Board of Internal Medicine. Dr. Kucuk has been a practicing in the field of medical oncology for over 27 years. His areas of expertise include cancer prevention, nutrition and cancer, chemoprevention, chemotherapy, medical oncology and clinical trials. (Kucuk ¶ 1.)

25. Dr. Kucuk conducts clinical research treating cancers of the prostate, bladder, kidney and testis. (Kucuk ¶ 2.)

26. He has authored or co-authored approximately 125 articles published in peer-reviewed scientific journals and more than 20 published book chapters and reviews. (Kucuk ¶ 3.)

27. Dr. Kucuk's report states that cancer is not a single disease but many different diseases, and there is no known treatment that is generally accepted as effective for all forms of cancer. (Kucuk ¶¶ 15, 32.)

28. Dr. Kucuk concludes that to support cancer treatment claims for a product, qualified experts in the field of oncology would require such claims to be supported by well-conducted, placebo-controlled, randomized, double-blind, clinical trials demonstrating the product's efficacy for the specific type(s) of cancer for which the claims are made. (Kucuk ¶¶ 32, 34.)

29. Dr. Kucuk's report details his review of the RAAX11 product label, the documents submitted by Respondents as substantiation for the RAXX11 product claims, and his own independent search of the existing scientific literature. (Kucuk ¶¶ 12, 13, 14, 16, 19, 20, 21, 50.)

30. After completing his review, Dr. Kucuk's expert opinion is that the existing body of scientific literature does not provide competent and reliable evidence that RAAX11, or either of its ingredients *Chrysobalanus icaco ("icaco")* and *Agaricus blazei murill ("agaricus")*, alone or in combination, has been scientifically proven to, or effectively can prevent, treat or cure any form of cancer. (Kucuk ¶¶ 12, 15, 50, 51.)

31. According to his expert report, Dr. Kucuk found no published scientific literature evaluating either RAAX11 or evaluating the combination of *icaco* and *agaricus* as a cancer treatment. (Kucuk ¶¶ 16, 17.)

32. Dr. Kucuk reported finding no published scientific literature evaluating the efficacy of RAAX11 or any clinical trial data with RAAX11. (Kucuk ¶ 16.)

33. Dr. Kucuk's search of the published scientific literature revealed no articles about the efficacy of taking the combination of *icaco* and *agaricus* as a cancer treatment, or even looking at potential mechanisms of anticancer activity. (Kucuk ¶ 17.)

34. In examining the ingredients in RAAX11separately, Dr. Kucuk found no published studies that evaluate *icaco* extract as a cancer treatment nor did he find a single human or animal study of *icaco*. (Kucuk ¶ 18.)

35. While Dr. Kucuk's report states that he found eight publications reporting the results of clinical or human studies using *agaricus,* he found no reports of properly conducted clinical trials regarding the efficacy of *agaricus* extract in patients with cancer. (Kucuk ¶ 20.)

36. Specifically evaluating the scientific literature in light of the allegations contained in the Commission's Complaint, Dr. Kucuk concluded that there is no scientific support for the claims that: (1) reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer (Complaint ¶ 6); (2) RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel (Complaint ¶ 8.A.); and (3) RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer (Complaint ¶ 8.B.). (Kucuk ¶¶ 11, 16, 51.)

37. After reviewing the materials submitted by Respondents as substantiation for their product claims, it is Dr. Kucuk's conclusion that the materials do not provide any data from randomized, placebo-controlled clinical trials with cancer patients and therefore, they do not provide any additional relevant clinical data to substantiate or otherwise support the cancer claims challenged in the Commission's Complaint for RAAX11. (Kucuk ¶ 50.)

38. Respondent Isely established and controlled a bank account for Gemtronics' business operations. Isely Ints. Resp. No. 18.

39. Respondent Isely acknowledged personally fulfilling the two orders for RAAX11 that were placed on the www.agaricus.net website by the FTC. Isely Dep. 57-59, 64.

40. Respondent Isely was personally identified on the Gemtronics packages, invoices, and in the promotional literature received by the FTC and admitted that these were his materials. S.D. 2 (Liggins Dec. ¶¶ 8, 9, 12, Atts. I, J; Isely Dep. 57-59, 64, 66-67, 69, 71, 74, 75-76.

41. Respondent Isely admitted that he received notices in the mail for the renewal of the domains that were registered in his name and he produced a renewal for "agaricus.net" that had been mailed to him. Isely Dep. 28; Respondent William Isely's Document Production Response, January 19, 2009, Exhibit 5 to Complaint Counsel's Exhibits, POD") Bates 0005.

42. Respondent Isely further admitted that when consumers purchase products on the www.agaricus.net using a credit card, that Isely gets the payment. Isely Dep. 123-24.

Dated: March 16, 2009

Respectfully submitted,

Barbara E. Bolton
Attorney for Complaint Counsel
Federal Trade Commission
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Atlanta, GA 30303
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404-656-1379 (facsimile)
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UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

In the Matter of **GEMTRONICS, INC.,** **a corporation, and** **WILLIAM H. ISELY,** **individually and as the owner of Gemtronics, Inc.**	**PUBLIC** **DOCKET NO. 9330**

[Proposed] ORDER GRANTING COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION

Having considered Complaint Counsel's Memorandum in Support of its Motion for Summary Decision and the Statement of Material Facts as to Which There is No Genuine Issue, and Respondents' opposition thereto,

IT IS HEREBY ORDERED that Complaint Counsel's Motion for Summary Decision, filed on March 16, 2009, is **GRANTED** consistent with the Proposed Order annexed hereto.

ORDERED:

_____
D. Michael Chappell
Administrative Law Judge

Dated:

UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

In the Matter of **GEMTRONICS, INC.,** **a corporation, and** **WILLIAM H. ISELY,** **individually and as the owner of Gemtronics, Inc.**	**PUBLIC** **DOCKET NO. 9330**

[Proposed] ORDER GRANTING COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION

For purposes of this order the following definitions apply:

1. "Commerce" shall mean "commerce" as defined in Section 4 of the FTC Act, 15 U.S.C. § 44.

2. "Competent and reliable scientific evidence" shall mean tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.

3. "Covered Product or Service" shall mean any dietary supplement, food, drug, or other health-related product, including, but not limited to, RAAX11, or any health-related service or program.

4. "Endorsement" means as defined in 16 C.F.R. § 255.0(b).

5. "Food" and "drug" shall mean "food" and "drug" as defined in Section 15 of the FTC Act, 15 U.S.C. § 55.

6. Unless otherwise specified, "respondents" shall mean:

A. Gemtronics, Inc., a corporation, and its successors and assigns and its officers; and

B. William H. Isely, individually and as the owner of Gemtronics, Inc;

and each of the above's agents, representatives, and employees.

I.

IT IS HEREBY ORDERED that respondents, directly or through any corporation, partnership, subsidiary, division, trade name, or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of RAAX11, or any substantially similar product or any other Covered Product or Service, in or affecting commerce, shall not represent, in any manner, directly or by implication, including through the use of a product name, endorsement, depiction, or illustration, that:

A. Such product is effective in the treatment or cure of cancer; or

B. Such product is effective in the prevention of cancer;

unless such representation is true, non-misleading, and, at the time the representation is made, respondents possess and rely upon competent and reliable scientific evidence that substantiates the representation.

II.

IT IS FURTHER ORDERED that respondents, directly or through any corporation, partnership, subsidiary, division, trade name, or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of any Covered Product or Service, in or affecting commerce, shall not make any representation, in any manner, directly or by implication, including through the use of a product name, endorsement, depiction, or illustration, about the efficacy, performance, or health-related benefits of any

Covered Product or Service unless the representation is true, non-misleading, and, at the time it is made, respondents possess and rely upon competent and reliable scientific evidence that substantiates the representation.

III.

IT IS FURTHER ORDERED that respondents, directly or through any corporation, partnership, subsidiary, division, trade name, or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of any Covered Product or Service, in or affecting commerce, shall not misrepresent, in any manner, expressly or by implication, including through the use of any product name or endorsement, the existence, contents, validity, results, conclusions, or interpretations of any test, study, or research.

IV.

IT IS FURTHER ORDERED that:

A. Nothing in this order shall prohibit respondents from making any representation for any drug that is permitted in labeling for such drug under any tentative or final standard promulgated by the Food and Drug Administration, or under any new drug application approved by the Food and Drug Administration; and

B. Nothing in this order shall prohibit respondents from making any representation for any product that is specifically permitted in labeling for such product by regulations promulgated by the Food and Drug Administration pursuant to the Nutrition Labeling and Education Act of 1990.

V.

IT IS FURTHER ORDERED that:

A. Respondents shall, within seven (7) days after the date of service of this order, deliver to the Commission a list, in the form of a sworn affidavit, of all consumers who purchased RAAX11 on or after May 2004 through the date of service of this order. Such list shall include each consumer's name and address, the product(s) purchased, and, if available, the consumer's telephone number and email address;

B. Within forty-five (45) days after the date of service of this order, respondents shall send by first class mail, postage prepaid, an exact copy of the notice attached as Attachment A to all persons identified in Part V.A. The face of the envelope containing the notice shall be an exact copy of Attachment B. The mailing shall not include any other documents; and

C. Except as provided in this order, respondents, and their officers, agents, servants, employees, attorneys, and representatives shall not sell, rent, lease, transfer, or otherwise disclose the name, address, telephone number, credit card number, bank account number, e-mail address, or other identifying information of any person who paid any money to any respondent, at any time prior to issuance of this order, in connection with the purchase of RAAX11. *Provided, however,* that respondents may disclose such identifying information to the FTC pursuant to Part V.A., above, or any law enforcement agency, or as required by any law, regulation, or court order.

VI.

IT IS FURTHER ORDERED that for a period of five (5) years after the last date of dissemination of any representation covered by this order, respondents shall maintain and upon request make available to the Federal Trade Commission for inspection and copying:

A. All advertisements and promotional materials containing the representation;

B. All materials that were relied upon in disseminating the representation; and

C. All tests, reports, studies, demonstrations, or other evidence in their possession or control that contradict, qualify, or call into question such representation, or the basis relied upon for the representation, including complaints and other communications with consumers or with governmental or consumer protection organizations.

VII.

IT IS FURTHER ORDERED that respondents shall deliver a copy of this order to all current and future principals, officers, directors, and managers, and to all current and future employees, agents, and representatives having responsibilities with respect to the subject matter of this order, and shall secure from each such person a signed and dated statement acknowledging receipt of the order. Respondents shall deliver this order to current personnel within thirty (30) days after the date of service of this order, and to future personnel within thirty (30) days after the person assumes such position or responsibilities.

VIII.

IT IS FURTHER ORDERED that respondent Gemtronics, Inc. and its successors and assigns shall notify the Commission at least thirty (30) days prior to any change in the corporation that may affect compliance obligations arising under this order, including but not limited to a dissolution, assignment, sale, merger, or other action that would result in the emergence of a successor corporation; the creation or dissolution of a subsidiary, parent, or affiliate that engages in any acts or practices subject to this order; the proposed filing of a bankruptcy petition; or a change in the corporate name or address. ***Provided, however***, that, with respect to any proposed change in the corporation about which respondent learns less than thirty

(30) days prior to the date such action is to take place, respondent shall notify the Commission as soon as is practicable after obtaining such knowledge. All notices required by this Part shall be sent by certified mail to the Associate Director, Division of Enforcement, Bureau of Consumer Protection, Federal Trade Commission, Washington, D.C. 20580.

IX.

IT IS FURTHER ORDERED that respondent William H. Isely, for a period of ten (10) years after the date of issuance of this order, shall notify the Commission of the discontinuance of his individual current business or employment, or of his individual affiliation with any new business or employment. The notice shall include the respondent's new business address and telephone number and a description of the nature of the business or employment and his duties and responsibilities. All notices required by this Paragraph shall be sent by certified mail to the Associate Director, Division of Enforcement, Bureau of Consumer Protection, Federal Trade Commission, Washington, D.C., 20580.

X.

IT IS FURTHER ORDERED that respondent Gemtronics, Inc., and its successors and assigns, and respondent William H. Isely shall, within sixty (60) days after the date of service of this order, and at such other times as the Federal Trade Commission may require, file with the Commission a report, in writing, setting forth in detail the manner and form in which they have complied with this order.

XI.

IT IS FURTHER ORDERED that this order will terminate twenty (20) years from the date of its issuance, or twenty (20) years from the most recent date that the United States or the Federal Trade Commission files a complaint (with or without an accompanying consent decree)

in federal court alleging any violation of the order, whichever comes later; ***provided, however***, that the filing of such a complaint will not affect the duration of:

A. Any paragraph in this order that terminates in less than twenty (20) years;

B. This order's application to any respondent that is not named as a defendant in such complaint; and

C. This order if such complaint is filed after the order has terminated pursuant to this paragraph.

Provided further, that if such complaint is dismissed or a federal court rules that the respondents did not violate any provision of this order, and the dismissal is either not appealed or upheld on appeal, then the order will terminate according to this paragraph as through the complaint was never filed, except that the order will not terminate between the date such complaint is filed and the later of the deadline for appealing such dismissal or ruling and the date such dismissal or ruling is upheld on appeal.

ATTACHMENT A

LETTER TO BE SENT BY FIRST CLASS MAIL

[To be printed on letterhead of Gemtronics, Inc./www.agaricus.net]

[Date]

To Whom It May Concern:

Our records show that you bought RAAX11 from our website www.agaricus.net. We are writing to tell you that the Federal Trade Commission ("FTC") has found that our advertising claims for these products were false or unsubstantiated, and has issued an Order prohibiting us from making those claims in the future. The Order entered against us also requires that we send you the following information about the scientific evidence on these products.

No scientific research has been done concerning the product RAAX11 as a prevention, treatment, or cure for cancer in humans. Very little scientific research has been done concerning either of the ingredients in RAAX11, *Chrysobalanus Icaco* extract and *Agaricus blazei Murill* mushroom extract, as a prevention, treatment, or cure for cancer in humans. The scientific studies that have been done do not demonstrate that RAAX11, or the ingredients in RAAX11, are effective when used as treatments for cancer.

It is very important that you talk to your doctor or health care provider before using ***any*** alternative or herbal product, including RAAX11. Speaking with your doctor is important to make sure that all aspects of your medical treatment work together. Things that seem safe, such as certain foods, herbs, or pills, may interfere or affect your cancer or other medical treatment, or other medicines you might be taking. Some herbs or other complementary or alternative treatments may keep your medicines from doing what they are supposed to do, or could be harmful when taken with other medicines or in high doses. It also is very important that you talk to your doctor or health care provider before you decide to take any alternative or herbal product, including RAAX11, instead of taking conventional cancer treatments that have been scientifically proven to be safe and effective in humans.

If you would like further information about complementary and alternative treatments for cancer, the following Internet web sites may be helpful:

1. The National Cancer Institute: www.cancer.gov/cancertopics/pdq; or
2. The National Center for Complementary and Alternative Medicines: www.nccam.nih.gov

You also can contact the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER or 1-800-422-6237.

Sincerely,

William H. "Bill" Isely
Gemtronics, Inc./www.agaricus.net

ATTACHMENT B

William H. Isely
Gemtronics, Inc./www.agaricus.net
964 Walnut Creek Road.
Franklin, North Carolina 28734

[name and address of purchaser]

GOVERNMENT ORDERED NOTICE

ORDERED:

D. Michael Chappell
Administrative Law Judge

Dated:

CERTIFICATE OF SERVICE

I hereby certify that on this date, I filed and served the attached:

1) COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION;
2) COMPLAINT COUNSEL'S MEMORANDUM IN SUPPORT OF MOTION FOR SUMMARY DECISION;
3) COMPLAINT COUNSEL'S STATEMENT OF MATERIAL FACTS AS TO WHICH THERE IS NO GENUINE ISSUE; and
4) [Proposed] ORDER GRANTING COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION

The original and one (1) paper copy via overnight delivery and one (1) electronic copy via email to:

Donald S. Clark, Secretary
Federal Trade Commission
600 Pennsylvania Ave., N.W., Room H-159
Washington, D.C. 20580
email: secretary@ftc.gov

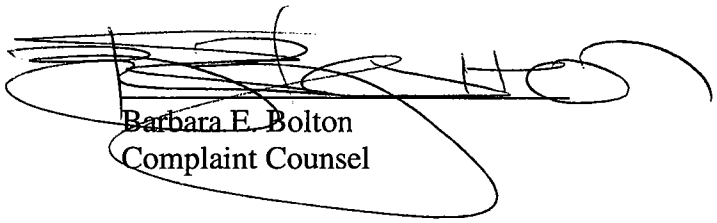
One (1) email copy and two (2) paper copies served by overnight mail delivery to:

The Honorable D. Michael Chappell
Administrative Law Judge
600 Pennsylvania Ave., N.W. Room H-112
Washington, D.C. 20580
email: oalj@ftc.gov

One (1) electronic copy via email and one (1) paper copy via overnight delivery to:

Matthew I. Van Horn
16 W. Martin Street, Suite 700
Raleigh, NC 27602
email: matthew@vanhornlawfirm.com

Dated: March 16, 2009



Barbara E. Bolton
Complaint Counsel

UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

In the Matter of **GEMTRONICS, INC.,** **a corporation, and** **WILLIAM H. "BILL" ISELY,** **individually and as the owner** **of Gemtronics, Inc.**	**DOCKET No. 9330** **Public Document**

EXHIBITS IN SUPPORT OF COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION

Attached hereto as Exhibits 1 through 5 are true and correct copies of documents produced by the parties and described below:

Exhibit 1: Respondents Isely's Answers to Interrogatories, and appended Exhibit A to the Interrogatories;

Exhibit 2: Declaration of FTC Investigator, Michael S. Liggins, and appended Attachments A through J;

Exhibit 3: Transcript of the Deposition of Respondent Isely and appended Exhibits;

Exhibit 4: Report of Dr. Omer Kucuk, Complaint Counsel's Expert and appended Attachments;

Exhibit 5: Document Production from Respondent Isely, Bates 00005

Dated: March 16, 2009

Respectfully submitted,

Barbara E. Bolton
Attorney for Complaint Counsel
Federal Trade Commission
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Atlanta, GA 30303
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404-656-1379 (facsimile)
bbolton@ftc.gov (email)

COMPLAINT COUNSEL'S EXHIBIT 1

UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

COMMISSIONERS: **William E. Kovacic, Chairman**
Pamela Jones Harbour
Jon Leibowitz
J. Thomas Rosch

PUBLIC

In the Matter of
GEMTRONICS, INC., **a corporation, and**
WILLIAM H. ISELY, **individually and as the owner of Gemtronics, Inc.**

DOCKET NO. 9330

RESPONDENT'S COUNSEL'S ANSWERS TO COMPLAINT COUNSEL'S FIRST SET OF INTERROGATORIES TO RESPONDENT WILLIAM H. ISELY

Pursuant to RULE OF PRACTICE 3.35, Respondent WILLIAM H. ISELY, by and through his undersigned counsel, hereby responds to Complaint Counsel's First Set of Interrogatories as follows:

INTRODUCTORY STATEMENTS AND GENERAL OBJECTIONS

1. WILLIAM H. ISELY has not fully completed his investigation into the facts pertaining to this suit, has not completed his discovery, and has not completed his preparation for trial. Answers contained herein are based only on such information and materials as are presently available and known to WILLIAM H. ISELY. This anticipated further discovery, investigation, legal research, and analysis may supply additional facts and will establish

information which may vary from that set forth herein. The answers set forth are given without prejudice to WILLIAM H. ISELY'S right to introduce evidence of any subsequently discovered fact[s] or circumstance[s]. WILLIAM H. ISELY accordingly reserves his right to change or modify any response as additional facts or circumstances are ascertained, analyses are made, and legal research is completed.

2. WILLIAM H. ISELY objects to Complaint Counsel's Interrogatories to the extent that the Interrogatories seek to impose requirements or obligations on WILLIAM H. ISELY in addition to or different from those imposed by the Code of Federal Regulations, Rules of Practice for Adjudicative Proceedings. In responding to each Interrogatory, WILLIAM H. ISELY will respond by providing only such information as may be required and proper under the Code of Federal Regulations, Rules of Practice for Adjudicative Proceedings.

3. WILLIAM H. ISELY objects to Complaint Counsel's Interrogatories to the extent that the Interrogatories seek information or documents that are protected from discovery by the attorney-client privilege, the work-product doctrine, confidential commercial information, or any other applicable privilege. Nothing contained in these responses is intended to, or in any way shall be deemed, a waiver of any such available privilege or doctrine. In responding to each Interrogatory, WILLIAM H. ISELY will not provide privileged or otherwise protected information.

4. The foregoing objections and limitations shall be applicable to, and included in, WILLIAM H. ISELY'S response to every definition and Interrogatory propounded by Complaint Counsel.

INTERROGATORIES

1. Identify and describe in detail the current and former duties, responsibilities, and work performed by you and others, either under your direction, supervision or otherwise, relating to advertising, promoting, offered for sale, sale, and distributing the product RAAX11, including but not limited to, providing an explanation of your day-to-day responsibilities and activities with respect thereto.

ANSWER: William H. Isely was the owner and operator of a sole proprietor business operating under the name Gemtronics which was a mail order dietary supplemental business. Mr. Isely had no employees and solely handled all necessary aspects required to operate a mail order dietary supplement business. He ordered products to stock, accepted orders by both mail and phone, filled orders, kept accounts, paid sales taxes as appropriate, as well as determining the income taxes to be paid resulting from income made by the business. In the year 2000, Takesun products were added to the line of products offered, adding the duties of importation from Brazil, which included additional interaction required with United States customs and the United States Federal Drug Administration, and custom brokers. Mr. Isely declined to sign as a Takesun distributor and purchases from Takesun by Mr. Isely were negotiated on a purchase by purchase basis with each transaction standing alone and not on the basis of any account.

Initial importation of RAAX11 was done under the name of "Nature First." Mr. Isely coordinated the content of a free web page of that name offered by Takesun to all wholesale buyers. For a period of seven months in 2001, Mr. Isely assumed the duties of senior partner of Takesun USA, a partnership established with a US citizen named Jane [Redacted for purposed of maintaining confidentiality], to import Takesun products to the US. This partnership was

dissolved in December of 2001, with the importation task transferred to Gemtronics but still ordering under the Name of Nature First since that name had been first used for importing. Jane's last name is withheld for the purposes of confidentiality, since her involvement was only prior to the sale of RAAX11.

The Web link from Takesun to Earth First became inoperative in 2002. In 2003, Mr. Isely operating under the name Gemtronics was registered as an approved FDA warehouse to comply with United States Homeland security requirements. In 2004, a free website offered by Takesun, our-agaricus.com, was established with no links to agarticus.net, and the importation and sale of RAAX11 was initiated. RAAX11 was imported until Mr. Isely was first contacted by Complaint Counsel. Once Mr. Isely was contacted by Complaint Counsel, Mr. Isely began ceasing to import RAAX11.

In 2006, Mr. Isely formed the corporation Gemtronics Inc. with the North Carolina Secretary of State as an organizer. Also in 2006, when Takesun renewed the registration of our-agaricus.com it, without the knowledge of Mr. Isely, Mr. Isely's name as registrant was attached to some of the Takesun web sites, including argaricus.net. A timeline of these events is shown in Exhibit A.

2. Identify and describe in detail the current and former duties, responsibilities, and work performed by you and others, either under your direction, supervision or otherwise, relating to the operations of the corporate respondent, Gemtronics, Inc., including but not limited to, providing an explanation of your day-to-day responsibilities and activities with respect thereto. Include a detailed description of your participation in the formation and operation of the corporate respondent, Gemtronics, Inc.

ANSWER: No actions were taken regarding Gemtronics, Inc. after it was formed with the North Carolina Secretary of State in 2006. It has remained an inactive corporation since its inception, only existing as a corporate shell. It has no shareholder or board members and has never been activated. It has never conducted any business or entered into any contracts. It has never obtained a federal tax identification number and has never filed taxes. To the extent the name "Gemtronics" has been utilized, it originated and has existed as an assumed name by Respondent William H. Isely, individually. However, Mr. Isely has never registered the assumed name "Gemtronics" with a Register of Deeds for any county in the state of North Carolina.

3. Identify and describe in detail the process by which, from whom, and the dates that you have obtained the product RAAX11 and any promotional literature for the product, including, but not limited to, identifying the amounts of product you obtained and the amount you paid for the product on each date.

ANSWER: Over a period from the middle of 2004 until approximately spring 2008 about 1150 bottles of RAAX11 were bought, usually from 12 to108 at a time, approximately 4 months apart, depending on sales. A few less were sold due to lost shipments and returns. Specific order information is not available in a timely manner as records are kept manually and are in storage. Very few were bought in 2004, peaking in 2005. Sales dropped off as competition entered the market. No literature was purchased for the products.

4. Identify each person consulted by you, or upon whose advice, opinion, or expertise you relied relating to advertising, promoting, offered for sale, sale, and distributing the product RAAX11, provide the substance of such advice, opinion, or expertise furnished to you and any compensation paid for such services.

ANSWER: I consulted with no one on these aspects of this business, being well versed in dietary supplement sales for over 30 years.

5. For each year from 2004 to the present, disclose the total amount of sales in terms of units and dollars that you have achieved for the sales of RAAX11 and identify the source producing the sale, including, but not limited to, the specific Internet website, newspaper advertisement, promotional mailing, etc. For each year, provide a total amount of sales, as well as, a break down amount of sales from each source.

OBJECTION: Respondent objects to this Interrogatory on the grounds that it is vague, overbroad. Respondent further objects to this Interrogatory on the ground that it seeks information that is neither relevant, nor reasonably calculated to lead to the discovery of admissible evidence.

ANSWER: Without waiving the afore-stated objections, Respondent states as follows:

Sales	year	# bottles sold	Gross sales Estimates	
	2004	19	$ 7,200	$ based on $400/bottle
	2005	370	44,400	subsequent years
	2006	147	17,640	based on $120/bottle
	2007	224	26,880	
	2008	158	18,960	

95% of orders were from repeat customers buying other products or referrals both contacting me by phone and email as I have been in the vitamin supplement business for approximately 30 years. 2 ½ % of orders were from www.our-agaricus.com. 2 ½ % of orders were by email from George Otto, generally for single bottle sample orders. None were direct from www.agaricus.net

RAAX11 sales Jan 1, 2004 to Dec 31, 2008

a. Total Bottles sold	1134
b. Number of purchases	325
c. Number of customers	115

d. Distributions of sales

1). One time buy of a single bottle	33
2). Customers who bought twice	18
3). Largest orders by number of bottlers	27 18 18 16 15 15 12 12 12
4). Largest customers by number of bot.	276 212 59 40 31 28

6. Identify and describe in detail any other payments you have received (other than the sales listed in response to Interrogatory No. 5), directly or indirectly, in connection with the advertising, marketing, promotion, sale and/or distribution of the product RAAX11 for each year from 2004 to the present. (This request includes the total dollar amount and source for each payments.)

OBJECTION: Respondent objects to this Interrogatory on the grounds that it is vague, overbroad. Respondent further objects to this Interrogatory on the ground that it seeks information that is neither relevant, nor reasonably calculated to lead to the discovery of admissible evidence.

ANSWER: Without waiving the afore-stated objections, Respondent states that it has not received any other payments directly or indirectly, in connection with the advertising, marketing, promotion, sale and/or distribution of the product RAAX11 for each year from 2004 to the present other than those identified in Interrogatory 5.

7. Identify and describe in detail the nature of your business relationship, and when and how you began doing business with Takesun do Brasil and/or George Otto, aka Georg Otto Kather, including, but no limited to, identifying all communications and any contracts or agreements, oral or written, any payments or other compensation, and the purchase or other provision of supplies, computer or other equipment, between you and Takesun do Brasil and/or George Otto. Also identify and describe in detail and any advertising or promotional material containing your name and Takesun do Brasil and/or George Otto.

ANSWER: Mr. Isely's relationship with Takesun do Brazil aka George Otto Kather was one of wholesale buyer from Manufacturer. Isely refused a distributor contract as the terms were ambiguous, expensive, and settlement of disputes would be impossible due to its being importation from a foreign country. Each purchase was individually negotiated on a stand-alone basis on price, method of shipment, and delivery. The relationship started in 2000 after Mr. Isely had bought sample quantities of Takesun products from intermittent dealers in the United States. Over a period of six (6) months the quantity imported grew to about $5,000 a month until the relationship was terminated in 2008 after Mr. Isely discovered his name had been used without his permission or knowledge to register internet Domains as well as to be a contact person on Takesun web sites. Mr. Isely is unable to recover most of the communications between himself

and Takesun, which took place over a period of nine (9) years, and which were routine dealings in the making of purchases in international commerce. Breaking down the business between RAAX11 and the nine other products is not possible. Mr. Isely refused any brochures and support material including computer materials as unusable in his US business for reasons of language as well as inappropriate medical claims since Mr. Isely's use was as dietary supplements only. Takesun did supply free web pages for two years and later a free domain, www.our-agaricus.com, as they did for anyone who bought from them in wholesale quantities. As a seller of Takesun products it was natural to mention the name Takesun do Brazil on Mr. Isely's brochure as the manufacturer of the products. This name was also on the products imported which were passed by the FDA. I received no other payments related to RAAX11 besides sales.

8. Identify and describe in detail the nature of your business relationship, and when and how you began doing business with Takesun USA, including, but no limited to, identifying all communications and any contracts or agreements, oral or written, any payments or other compensation between you and Takesun USA, and any advertising or promotional material containing your name and Takesun USA.

ANSWER: In 2001, Mr. Isely's largest customer, Jane [Redacted] wanted to become a partner with Mr. Isely. He and Jane [Redacted] formed Takesun USA and registered with a Fed. ID #. 565-226-1206. Mr. Isely's duties were to import products and his partner Jane was to warehouse products and ship to retail sellers, which turned out to be only Jane [Redacted] and myself. Mr. Isely and Jane envisioned other retail sellers who did not materialize. Coordination

with the West coast was difficult and there was not enough income for two people. As such, the partnership was dissolved before the end of 2001. Jane [Redacted] continued retail.

During the period of the partnership with Jane, Mr. Isely operated two separate business, Takesun USA and Gemtronics. Takesun USA imported products and the products were paid for by Mr. Isely and myself and Jane. Gemtronics bought products from Takesun USA and sold them at retail. This was before the era of RAAX11. The relationship of Mr. Isely to various assumed business names is shown within the attached Exhibit "A".

9. Describe in detail any communications and any contracts or agreements, oral or written, that you have had with any companies or individuals related to advertising, promoting, offering for sale, sale and/or distribution of RAAX11.

ANSWER: Other than the brief partnership with Jane [Redacted] Mr. Isely has had no contracts, agreements, oral or written with any individuals related to advertising, promoting, offering for sale, sale or distribution of RAAX11. This excludes the normal conduct of business of selling, giving prices, etc. of a mail order/phone business.

10. Disclose the total amount of dollars that you have spent to advertise, market, or otherwise promote the product RAAX11 for each year from 2004 to the present, broken down by each medium used (i.e., print, Internet, radio, or other means). (This request includes, but is not limited to, all expenditures attributable to the creation, development, evaluation, approval, modification, and dissemination of promotional materials).

ANSWER: Mr. Isely has spent no money advertising RAAX11 beyond the small percentage of space it takes up in my brochure which I print myself. Ink and paper for the brochure probably runs $40/year so 10% allocated to RAAX11 would be $4.

11. Describe in detail your participation in the Internet website www.agaricus.net, including, but not limited to, the registration for the domain "agaricus.net," the use of your name and telephone numbers appearing on the website, testimonials from you appearing on the website, and the solicitation for participation in an ongoing study in the USA of RAAX11 appearing on the website. Also include the date you began receiving orders for RAAX11 placed on the Internet website www.agaricus.net, how you received these orders, how these orders were filled by you, how you received payment for such orders, and how much you were paid.

OBJECTION: Respondent objects to this Interrogatory on the grounds that it is vague, overbroad. Respondent further objects to this Interrogatory on the ground that it seeks information that is neither relevant, nor reasonably calculated to lead to the discovery of admissible evidence.

ANSWER: William H. Isely had no involvement with the website www.agaricus.net & did not register www.agaricus.net under his name; that was done by mistake by some member of the staff of Takesun do Brasil. William H. Isely's name, address and telephone number appearing for contact purposes included on the website, appeared on www.agaricus.net without his knowledge or permission. William H. Isely gave George Otto permission to use the testimony about his health records, but not specifically for use on the website www.agaricus.net.

William H. Isely was not aware that his name had been linked to a study involving RAAX11 and he was not involved in any such study. William H. Isely did not know that he ever received any orders for RAAX11 from the website www.agaricus.net, having no interface with the website. On rare occasions he would receive an email from George Otto asking him to drop

ship a sample order, but he had no indication on such orders as to their source. He generally did not receive payment for such small orders.

12. Describe in detail your participation in any other Internet websites, including, but not limited to, your name, address and/or telephone number appearing on the registration for any domain, and any links between websites, i.e., for ordering RAAX11.

ANSWER: The only website Mr. Isely participated in during the time RAAX11 was for sale was www.our-agaricus.com in which his name was given as the registrant. This website had no link to other websites, such as www.agaricus.net.

13. Identify and describe in detail all oral and written communications, including email, you have had with the U.S. Food and Drug Administration including, but not limited to any communications concerning warehouse, facility, or other registrations you have had with the agency, and concerning the agency's letter to you dated April 2008.

ANSWER: Mr. Isely did not keep records between himself and the FDA, particularly since most were by telephone. Some stand out in memory, based upon information and belief:

a. Mr. Isely's first large import order, probably in 2000, was held by the FDA for improper labeling. Mr. Isely redesigned the labels to be in accordance with the FDA Labeling Act. Takesun printed new labels and Mr. Isely arranged for his broker to re-label the products under the watchful eye of FDA inspectors. There were numerous letters, phone calls and package shipments over a period of six (6) weeks.

b. As a result of the Homeland Security Act, Mr. Isely registered Gemtronics, Inc. as an FDA approved warehouse.

c. Perhaps one shipment in ten was selected for special inspection and/or product testing for purity, contamination, etc. They always passed.

d. Perhaps another shipment in ten would be held because the FDA inspector was not familiar with the product and for clearance required that they be given botanical names and plant descriptions before clearance.

e. When Mr. Isely was expecting an order he would check and see that the Prior Notice had been filed by Takesun or his shipper.

f. The last shipment received in the spring/summer of 2008 was held for a month before Mr. Isely was informed that the identification of the preservative used was not given on the label. After several discussions the FDA released the shipment with the understanding that the label would be modified before the next shipment.

Regarding the FDA letter April 2008, it was properly served upon Mr. Isely requiring a return receipt rather than being sent to www.agaricus.net by email. It was a warning that paralleled the one from the FTC, which was never served. It was answered through counsel providing the same evidence that was initially given the FTC that Mr. Isely does not participate in the control/management of www.agaricus.net and that his name and contact information were used without his knowledge or permission, including domain registrations, with the exception that www.agaricus.net could refer inquiries to Mr. Isely regarding his medical history with prostate cancer. Mr. Isely provided the FDA with George Otto Kather's name as their contact person with several email addresses, asked Takesun to correct their web site registrations, take his name off their web sites, and stop selling products to the US. Eventually the FDA wrote Mr. Isely a letter thanking him for his cooperation. Subsequently Phillip Campbell, when queried by a local news organization about Mr. Isely's case, said in equivalent words that Mr. Isely was innocent and since they had no leverage they were not pursuing the case.

14. Disclose the name, address, and telephone number of each consumer either that

has purchased the product RAAX11 from you or to whom you have shipped the product RAAX11, and provide the amount each consumer purchased in terms of total number of bottles and total amounts paid for the product.

OBJECTION: Respondent objects to this Interrogatory on the grounds that it is vague, overbroad. Respondent further objects to this Interrogatory on the ground that it seeks information that is neither relevant, nor reasonably calculated to lead to the discovery of admissible evidence. Respondent further objects on the basis that the information sought contains confidential information of third parties who provided said information with an expectation of privacy.

ANSWER: Based on the above-foregoing objections, Mr. Isely respectfully submits no response to this Interrogatory.

15. Identify and describe in detail all oral and written communications, including email, you received, from consumers concerning the marketing and sale of the product RAAX11 and/or the participation in a study of RAAX11, including disclosing the total amount of refunds requested by consumers and the total amount of refunds to consumers, in terms of units and dollars, that you have made for RAAX11 for each year from 2004 to the present.

OBJECTION: Respondent objects to this Interrogatory on the grounds that it is vague, overbroad. Respondent further objects to this Interrogatory on the ground that it seeks information that is neither relevant, nor reasonably calculated to lead to the discovery of admissible evidence. Respondent further objects on the basis that the information sought contains confidential information of third parties who provided said information with an expectation of privacy.

ANSWER: Without waiving the objection, Mr. Isely states as follows:

Mr. Isely has no records of people asking about marketing or sale of RAAX except the normal business questions of price and delivery terms. Perhaps two potential customers asked about participating in a study to get a lower price and Mr. Isely told them that he was not part of a study, nor did he know of one. One customer wanted a refund when he changed his mind after placing an order and it had been shipped. Mr. Isely wanted him to pay for shipping, but he eventually paid the whole thing. One UK customer took delivery of a large order and gave a delivery receipt to the express company. Later she reversed the charge on her credit card telling the CC bank the order had not been delivered. Being a foreign customer, Mr. Isely had no recourse. For about six customers whose relatives had bought products and then later died, Mr. Isely provided refunds for the unused items.

16. Identify and describe in detail all reliable scientific evidence that demonstrates that RAAX11 is effective in the prevention and cure of cancer.

ANSWER: Mr. Isely has not seen data that provides a double blind quality study.

17. Identify and describe in detail all evidence that you relied upon to substantiate the representations that RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel; and that RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer.

OBJECTION: Respondent objects to this Interrogatory on the grounds that it is vague, overbroad. Respondent further objects to this Interrogatory on the ground that it seeks information that is neither relevant, nor reasonably calculated to lead to the discovery of admissible evidence.

ANSWER: Respondent did not substantiate the representations that RAAX11 is

effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel; and that RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer.

18. Identify by name, address, and account number any bank or other financial accounts that received or disbursed funds relating to the marketing, purchasing, sale, and/or distribution of the product RAAX11. Explain what responsibilities you exercised, or had the authority to exercise, for those bank or other financial accounts, including the names of persons with who you shared the authority, and the type of transactions that were processed through each account.

ANSWER: Bank account for period RAAX11 was sold

Bank account in the assumed name of Gemtronics [account number redacted].

Bank name RBC Centura
Franklin, NC, 28734

William H. Isely was authorized to perform all actions associated with the account

Transactions were deposits of purchasers and payouts for expenses including the purchase of products from Brazil. Occasional profits were paid to owner.

Account was terminated in the fall of 2008 after the destruction of the business.

19. Provide the name and location of any other corporation or business entity in which you hold or held ownership, directorship, or other position of responsibility.

ANSWER: None.

20. Provide a detailed background, regarding your education, including any professional degrees or licenses that you hold, and employment history, including the name and location of your employers and dates of employment.

ANSWER: BSME, MSME

Westinghouse, Pittsburg, Baltimore , 1948 to 1953

Boeing Aircraft Co. Cape Kennedy, Fla 1953 to 1955

Honeywell Corp, St. Petersburg, Fla, 1955 to 1987

21. Identify the name and address of the owner of the following telephone numbers: A) 866-944-7359; B) 828-369-7590; and C) 828-369-5861.

ANSWER: William H. Isely.

22. Identify and describe in detail all advertising, promotional literature, and other marketing or promotional material disseminated by you or which include your name, telephone number, or other contact information for you.

ANSWER: A product brochure which shows about 10 imported Takesun products that depicts price image, and a brief description of the contents. This product brochure includes a link to Nature First, which was discontinued approximately. This brochure also makes mention of Takesun USA, the importing partnership referred to above that was dissolved in approximately as described in previous responses to Interrogatories.

This the 3rd day of February, 2009.

LAW OFFICE OF
MATTHEW I. VAN HORN, PLLC

By _____
MATTHEW I. VAN HORN
N. C. Bar No. 26166
16 West Martin St., Suite 700
Raleigh, NC 27601
Telephone: (919) 835-0880
Facsimile: (919) 835-2121

Attorney for Respondents

VERIFICATION

NORTH CAROLINA)
) **SS.**
WAKE COUNTY)

WILLIAM H. ISELY, being first duly sworn, deposes and says that he is the Respondent in the above entitled action, that he has read the foregoing document and knows the contents thereof; that the same is true of its own knowledge except for those matters and things stated on information and belief and as to those he believes them to be true.

This the _____ day of February, 2009.

WILLIAM H. ISELY

SUBSCRIBED and SWORN to before me
this _____ day of February, 2009.

NOTARY PUBLIC

Printed Name **NOTARY PUBLIC**

My Commission expires:_____

CERTIFICATE OF SERVICE

This is to certify that the undersigned has this date served this **RESPONDENTS' COUNSEL'S ANSWERS TO COMPLAINT COUNSEL'S FIRST SET OF INTERROGATORIES TO RESPONDENT WILLIAM H. ISELY** in the above entitled action upon all other parties to this cause by facsimile and by depositing a copy hereof in a postpaid wrapper in a post office or official depository under the exclusive care and custody of the United States Postal Service, properly addressed to the attorney or attorneys for the parties as listed below.

Ms. Barbara E. Bolton
Federal Trade Commission
225 Peachtree Street, N.E.
Suite 1500
Atlanta, GA 30303

This the 3rd day of February, 2009.

MATTHEW I. VAN HORN

EXHIBIT A

William H. Isely Relationship..to Various AKA's

Year	Gemtronics	Nature First	Takesun USA
1993	Registered 7-7-1993 with NC to act as a mail order supplier of dietary supplements		
2000	Added Takesun products to those already carried by Gemtronics	Began importing for WHI Under name of Nature First. Also had Web site arrived at by Clicking "US sales" on Agaricus.net	
2001			Formed Partnership with Jane, June '01, Fed ID 56-2261206 To import from Takesun. Dissolved partnership Dec. '01
2002	Business was conducted Without web site support	Link to Agaricus.net was terminated when web site became non functional	
2003	Because of confusion at Takesun do Brasil shipments were made to Wm. H., Isely variously addressed to Wm H.Isely, Gemtronics, Nature First & combinations,		
	All functions of business Consolidated under Gemtronics	FDA registration was done Under Nature first, registra- # 10827550148	
2004	Web Site Our-agaricus initiated in June Importation of RAAX11 begun		
2005			
2006	*Gemtronics Inc* registered. Domain our-agaricus Registration renewed. By mistake G. Otto listed the registrant for three of his web sites as William Isely		
2007			
2008	With Gemtronics business destroyed, the domain our-agaricus was no longer useful and was allowed to lapse. Another business is now using this domain, Gemtronics registration with NC as a merchant is expected to lapse Dec. 31, 2008.		

COMPLAINT COUNSEL'S EXHIBIT 2

DECLARATION OF MICHAEL S. LIGGINS
Pursuant to 28 U.S.C. § 1746

I, Michael S. Liggins, hereby state that I have personal knowledge of the facts set forth below. If called as a witness, I could and would testify as follows:

1. I am a citizen of the United States and am over the age of 21. I am employed by the Federal Trade Commission ("FTC" or "Commission") in the Southeast Region as an Investigator. The business address of the Federal Trade Commission, Southeast Region, is 225 Peachtree Street, NE, Suite 1500, Atlanta, Georgia 30303. I have been employed by the FTC since 2000 and joined after serving 19 years as a Criminal and Military Investigator and sworn peace officer. I have personal knowledge of the facts stated herein and, if called, would testify to same.

2. As an Investigator with the FTC, my duties include investigating parties who are suspected of engaging in unfair or deceptive acts or practices in violation of the Federal Trade Commission Act, as well as acts or practices in violation of other statutes enforced by the FTC. My duties include performing investigative tasks and computer research using a variety of Internet search engines, public record and law enforcement databases, and software-based investigative tools. I am also the custodian of documents and records obtained by the FTC during the course of investigations to which I am assigned.

3. As part of my duties as an Investigator for the FTC, I participated in the investigation of the activities and business practices of Gemtronics, Inc. ("Gemtronics") and William Isely ("Isely") (collectively hereinafter "Respondents") involving the advertising, marketing and sale of the product "RAAX11."

CIVIL INVESTIGATIVE DEMAND TO VERIZON COMMUNICATIONS, INC.

4. A Civil Investigative Demand ("CID") was issued to Verizon Communications,

Inc. ("Verizon") for information about three telephone numbers associated with Respondents Gemtronics and Isely. In response to the CID, Verizon produced telephone records to the FTC for the telephone numbers (828) 369-7590 and (828) 369-5861 (North Carolina exchanges); and (866) 944-7359 (a toll-free number). These records contain account subscriber information that list William Isely as the owner of the telephone numbers with service provided at 964 Walnut Creek Road, Franklin, NC 28734. (**Attachment A**, FTC Bates #s ("FTC-") 000206 - 210.)

INTERNET DOMAIN REGISTRATIONS

5. As part of my investigation, I conducted a search and examination of the WHOIS database on December 20, 2007. My search revealed that:

A. Respondent Isely is listed as the registrant, and administrative and technical contact for the domain "agaricus.net" at 964 Walnut Creek Road, Franklin, NC 28734. (**Attachment B**, FTC-000157 - 159);

B. Respondent Isely is listed as the registrant, and administrative and technical contact for the domain "our-agaricus.com" at 964 Walnut Creek Road, Franklin, NC 28734. (**Attachment B**, FTC-000161 - 163); and

C. Respondent Isely is listed as the registrant, and administrative and technical contact for the domain "opc-agaricus.net" at 964 Walnut Creek Road, Franklin, NC 28734. (**Attachment B**, FTC-00032 - 34.)

INTERNET ADVERTISING

6. As part of my investigation, I conducted a search and examination of various Internet search engines for websites containing either the words Isely, Gemtronics and/or the telephone numbers belonging to Respondent Isely, and RAAX11. My search revealed the following information:

www.agaricus.net

A. On December 12, 2007, I found advertisements for RAAX11 that also included Respondent Isely's name and telephone numbers on the universal resource locator (URL) www.agaricus.net. On that same date, December 12, 2007, I reviewed and preserved to a CD an exact copy of this website. (**Attachment C** is copy of the CD containing the captured website.) Exhibit B to the Commission's Complaint in this matter is taken from the CD that is **Attachment C**, dated December 12, 2007.

B. On December 13, 2007, I printed out copies of webpages directly from captured CD of the website. Some of the webpages that included RAAX11 and either references to Respondent Isely and/or his telephone numbers are appended hereto as **Attachment D** (FTC-00124 - 25, 137 - 141);

C. On January 3, 2008, I found advertisements for RAAX11 that also included the name and telephone numbers for Respondent Isely on the website www.agaricus.net. I reviewed and preserved to a CD an exact copy of this website. (**Attachment E** is a copy of the CD containing the captured website.) Exhibits A, C, and D to the Commission's Complaint in this matter are taken from the CD that is **Attachment E**, dated January 3, 2008;

D. On January 30, 2008, I went to the website www.agaricus.net and printed out copies of webpages directly from the website. Some of the webpages that included RAAX11 and either references to Respondent Isely and/or his telephone number are appended hereto as **Attachment F** (FTC-00114 - 117);

E. At each time that I reviewed the website www.agaricus.net, the only telephone

numbers that I found listed on the website for information on, or product ordering for RAXX11 in the United States were those belonging to Respondent Isely (listed in ¶ 4, above).

www.our-agaricus.com

F. On December 13, 2007, I went to the website www.our-agaricus.com and printed out copies of webpages directly from the website. Some of the webpages that included RAAX11 and references to Gemtronics, Respondent Isely and/or his telephone number are appended hereto as **Attachment G** (FTC-00170 - 172, 175 - 176).

www.takesun.com

G. On December 20, 2007, and again on April 18, 2008, I went to the website www.takesun.com and printed a webpage directly from the website. The webpage included the statement "FDA registered Warehouse Franklin/USA." This webpage further stated "[l]ooking for distributors - contact us for details" and Respondent Isely's toll-free telephone number, (866) 944-7359. These webpages printed on December 20, 2007, and April 18, 2008, are appended hereto, respectively, as **Attachment H** (FTC-00193 and 194).

FTC UNDERCOVER PURCHASES

First Purchase of RAAX11 from www.agaricus.net

7. On January 3, 2008, as part of my investigation, I accessed the Internet and typed the URL www.agaricus.net which allowed me access to the website www.agaricus.net. I then went to the product order page and ordered one 100ml bottle of RAAX11, for a total cost of $134.90 (including shipping), using the name and address, Riece Miles, [redacted address],

Lorton, VA 22079. The transaction was completed online by establishing and utilizing a PayPal e-commerce account. The PayPal transaction identification number for the RAAX11 purchase was 20U8900657657914S. **Attachment I** (FTC-00013 - 15) is a copy of the Internet order form and transaction receipt.

8. On January 17, 2008, I received, via Federal Express, the Gemtronics order from Diana Finegold, a Paralegal Specialist assigned to the FTC's Division of Advertising Practices, 600 Pennsylvania Ave, Washington, D.C. 20580. Ms. Finegold manages the FTC's undercover mail address located on [redacted address] in Lorton, VA.

9. The package containing the bottle of RAAX11 was mailed by U.S. mail from Franklin, NC and listed William Isely, 964 Walnut Creek Road, Franklin, NC 28734 as the sender. **Attachment I** (FTC-00017) is a copy of the package envelope. When I opened and examined the contents of the package, the bottle of RAAX11 was damaged and the product had spilled out over the contents of the package which included a Gemtronics invoice and promotional literature rendering these pages difficult to read. However, the invoice included in the package was from Gemtronics at 964 Walnut Creek Road, Franklin, NC 28734, and included Respondent Isely's telephone number and email address. The invoice also identified William Isely as the general manager of Takesun USA and Gemtronics for retail sales. **Attachment I** (FTC-00019) is a copy of the package invoice.

Second Purchase of RAAX11 from www.agaricus.net

10. On January 23, 2008, as part of my investigation, I accessed the Internet and typed the URL www.agaricus.net which allowed me access to the website www.agaricus.net. I then went to the product order page and ordered one 100ml bottle of RAAX11, for a total cost of $134.90 (including shipping), using the name and address, Dana Long, [redacted address],

Roanoke, VA 24018. The Internet confirmation webpage from the website stated: "Your Credit Card is charged using a SSL secured server. On your statement will appear "GEMTRONICS SECURE PAYMENTS." **Attachment J** (FTC-00029) is a copy of the webpage confirmation for the purchase. The transaction then was completed online by establishing and utilizing a PayPal e-commerce account. The PayPal transaction identification number for the RAAX11 purchase was 00061355NC651964H. **Attachment J** (FTC-00028, 30 - 31) is a copy of the Internet order form and transaction receipt.

11. On February 1, 2008, I received, via Federal Express, the Gemtronics order from Lynne Colbert, an Investigator assigned to the FTC's Division of Advertising Practices, 600 Pennsylvania Ave, Washington, D.C. 20580. Ms. Colbert manages the FTC's undercover mail address located on [redacted address] in Roanoke, VA.

12. The package containing the bottle of RAAX11 was mailed by U.S. Express Mail from Franklin, NC and listed William Isely and Gemtronics at 964 Walnut Creek Road, Franklin, NC 28734 as the sender. **Attachment J** (FTC-00022) is a copy of the package envelope. I opened and examined the contents of the package, which contained a bottle of RAAX11, a Gemtronics invoice, and promotional literature for RAAX11. **Attachment J** (FTC-000198) is a copy of the RAAX11 bottle label. The package invoice was from Gemtronics at 964 Walnut Creek Road, Franklin, NC 28734, and listed Respondent Isely's telephone number and email address as well as a note from him asking that future orders be placed with him directly by phone or email. **Attachment J** (FTC-00021) is a copy of the package invoice. The promotional literature included in the package from Gemtronics consisted of three printed color pages. The first promotional page includes the heading "Takesun U.S.A." and information about agaricus mushrooms. This page directs consumers to go to the website www.agaricus.net and

"click on USA sales," or the website www.our-agaricus.com and lists Gemtronics and a telephone number and an email address for Respondent Isely to obtain more product information. **Attachment J** (FTC-00024) is a copy of the first promotional page. A second promotional page, entitled "Popular Products," lists RAAX11 for sale at the price of $119 per 100ml bottle, as well as other agaricus products for sale. **Attachment J** (FTC-00025) is a copy of the second promotional page. The third promotional page, entitled "RAAX11/Agaricus OPC Protocol Description and Results," makes a number cancer-related treatment claims for RAAX11. This page directs consumers to contact William Isely for more information at his email address or telephone number, which are also provided on this page. **Attachment J** (FTC-00026) is a copy of the third promotional page.

I declare under penalty of perjury that the foregoing statement is true and correct. Executed this 12th day of March 2009.

Michael S. Liggins

Michael S. Liggins, Investigator
Federal Trade Commission
Southeast Region

ATTACHMENT A

VERIZON LEGAL COMPLIANCE
P O BOX 1001 6TH FLOOR NORTH
SAN ANGELO, TX 76902

TO: BARBARA BOLTON
COMPANY: FEDERAL TRADE COMMISSION ATLANTA
FAX NUMBER: 4046561379
PHONE NUMBER: 404-656-1366
FROM: VZLC JW
DATE: 06/02/2008 01:23:59

STARSxp Case Number: 08278428000

Docket/File Number: 0023191

Faxed Pages: 16

SENDER'S PHONE NUMBER: 1-888-483-2600

SENDER'S FAX NUMBER: 325-949-6916
Notes/Comments:

---------- SUBSCRIBER REPORT ----------

Case #: 08278428000 Phone #: 8283697590

STARSxp Case Number 08278428000
TN: 8283697590 MSD: Original Acct DT: 19880622
Primary BTN: 8283697590 Account Status: L
Class of Service: R Local Service Provider:
Cust Acct Num: 3562003072
Service Date: 20071214 Service Order Num: C0812474
Service Term Date:
Billing Company Code: CTNC
PUB/NON:

Customer Name: ISELY, WILLIAM H
Service Address: 964 WALNUT CRK RD FRANKLIN NC 28734-9533 null
Service Location:
Service City: FRANKLIN
Service State: NC
Service Zip Code: 287349533

Listing Name: Isely, William H
Listing Address: 80, , Walnut Ck Rd
Listing Location:

Case #: 08278428000 Phone #: 8283695861

**** No Current Records were found for Telephone #: 8283695861

Case #: 08278428000 Phone #: 8669447359

WILLIAM ISELY
964 WALNUT CREEK RD
FRANKLIN, NC 28734
SERVICE DT: 03/01/2001
FINAL DT: 05/27/08

---------- DATED SUBSCRIBER REPORT ----------

Case #: 08278428000 Phone #: 8283695861

Service dt: 19960626
WILLIAM H ISELY
964 WALNUT CREEK RD
FRANKLIN NC 28734-9533
Final dt: 20071214

---------- SERVICE & EQUIPMENT REPORT ----------

Case #: 08278428000 Phone #: 8283697590

STARSxp Case Number 08278428000
TN: 8283697590
Primary BTN: 8283697590
InterLATA Freeze PIC Indicator: O
InterLATA CarrierName Abbrev :
InterLATA Presubscription Indicator Code: 05483
InterLATA PresubIXC EffvDt: 20071214
InterLATA PresubIXCSt Code: 1
Internatl Freeze PIC Indicator:
International Presubscription Indicator Code:
Internatl Presub Prvdr Effv Dt:
Internatl Presub Status Code:
IntraLATA Freeze PIC Indicator: O
IntraLATA Carrier Name Abbrev:
IntraLATA Presubscription Indicator Code: 05448
IntraLATA Presub Prvdr EffvDt: 20071214
IntraLATA Presub Status Code: 1

Feature Code:	Feature Code Description:
00372	ADL LSTG
00506	VZLD- VERIZON FREEDM DISPLAY
04778	CALLR ID W/ACB
07517	VOL TRACKING
07518	VOL TRACKING-SHADOW
20070	INTER ACC CHRG SGL LN
38882	VZ FREEDOM ESSENTIALS - BNDL
38883	VZ FREEDOM ESSENTIALS
38884	LEC PRDUCTS GROUP- VZ FR ESS
38892	UNL LCL TOLL/VZ FR ESS
38903	UNL LCL TOLL/VZ FR ESS - TRK
40259	CW/CCW
40613	3-WAY CALL
40667	CALL FWD
61663	TPP-NO
74864	SGL LN FLAT
87002	IWMN INSIDE W MNTNC NO
38900	UNL LD/VZ FR ESS
38911	UNL LD/VZ FR ESS - CHRG
82546	INTERNATIONAL OCP DENIED

---------- BILLING ADDRESS REPORT ----------

Case #: 08278428000 Phone #: 8283697590

STARSxp Case Number 08278428000
TN: 8283697590
Primary BTN: 8283697590
Billing Name: ISELY, WILLIAM H
Billing Address: 964 WALNUT CRK RD FRANKLIN NC 28734-9533
Billing City: FRANKLIN
Billing State: NC
Billing ZipCode: 287349533

ATTACHMENT B

NetworkSolutions

Login

Customer Service
Call us toll free

Your cart is empty

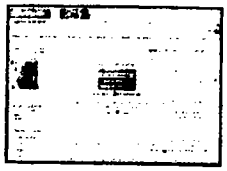
WHOIS Search Results

Available **agaricus** extensions:

.tv	.bz
☐	☐

Order Selected Domain(s)

Your WHOIS Search Results



agaricus.net
Services from Network Solutions:

Certified Offer Service - Let us help you get this domain name!

Backorder - Try to get this name when it becomes available.

SSL Certificates - Get peace of mind with a secure certificate.

Enhanced Business Listing - Promote your business to millions of viewers for only $1 a month!

This WHOIS database is provided for information purposes only. We do not guarantee the accuracy of this data. The following uses of this system are expressly prohibited: (1) use of this system for unlawful purposes; (2) use of this system to collect information used in the mass transmission of unsolicited commercial messages in any medium; (3) use of high volume, automated, electronic processes against this database. By submitting this query, you agree to abide by this policy.

Registrant:
William Isley
964 Walnut Creek Rd
Franklin, NC 28734-9533
US

Domain Name: AGARICUS.NET

Administrative Contact, Technical Contact, Zone Contact:

William Isley
George Otto
964 Walnut Creek Rd
Franklin, NC 28734-9533
US
(828)389-7590
gotto@takesun.com

Domain created on 13-Jun-1998
Domain expires on 12-Jun-2008
Last updated on 26-Nov-2007

Domain servers in listed order:

DNS1.SUPREMEDNS.COM
DNS2.SUPREMEDNS.COM

The previous information has been obtained either directly from the registrant or a registrar of the domain name other than Network Solutions. Network Solutions, therefore, does not guarantee its accuracy or completeness.

Show underlying registry data for this record

Current Registrar:	DOMAINDISCOVER
IP Address:	209.25.170.23 (ARIN & RIPE IP search)
IP Location:	UK(UNITED KINGDOM)
Record Type:	Domain Name
Server Type:	Apache 2
Lock Status:	clientTransferProhibited
Web Site Status:	Active
DMOZ	1 listings
Y! Directory:	see listings
Web Site Title:	~Agaricus blazei Murill - Alternative Therapies
Meta Keywords:	Agaricus blazei Murill, Mushrooms, Alternative Cancer Therapies, HIV, Free Visits, Icacopflaume,Chrysobalanus icaco <meta name=
Secure:	No
E-commerce:	No
Traffic Ranking:	Not available
Data as of:	13-Sep-2005

C IP Address

Search

Need to get your business online?
Our professional designers can build a custom Web site for your business.
$11.95/month, plus a $499.00 design fee

Go

PerformanceClicks™ from Network Solutions
Create and manage your pay per click advertising from as low as **$125/month** plus **$99 one time set-up fee**

Go

"An outstanding customer service experience" J.D. Power and Associates

EDITORS' CHOICE

SiteSafe $1M GUARANTEE EXTENDED Network Solutions

100% Secure Transaction

For your protection, this Web site is secured with the highest level of SSL Certificate encryption.

NetworkSolutions.

Login

Customer Service
Call us toll free

Your cart is empty

WHOIS Search Results

Available **our-agaricus** extensions:

.net	.org	.mobi	.info	.biz	.de	.tv	.co.uk	.eu	.bz
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Order Selected Domain(s) >

Your WHOIS Search Results

IMAGE NOT AVAILABLE

our-agaricus.com
Services from Network Solutions:

Certified Offer Service - Let us help you get this domain name!
Backorder - Try to get this name when it becomes available.
SSL Certificates - Get peace of mind with a secure certificate.
Enhanced Business Listing - Promote your business to millions of viewers for only $1 a month!

In most cases, the Registrar is not the owner of domain names listed in this database.

Registrant:
William Isely
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States

Registered through: Cheap-DomainRegistration.com
Domain Name: OUR-AGARICUS.COM
Created on: 01-Jul-04
Expires on: 01-Jul-08
Last Updated on: 17-Jun-07

Administrative Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
8283697590 Fax --

Technical Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
8283697590 Fax --

Domain servers in listed order:
DNS1.SUPREMECENTER20.COM
DNS2.SUPREMECENTER20.COM

The previous information has been obtained either directly from the registrant or a registrar of the domain name other than Network Solutions. Network Solutions, therefore, does not guarantee its accuracy or completeness.

Show underlying registry data for this record

Current Registrar: WILD WEST DOMAINS, INC.
IP Address: 209.25.170.23 (ARIN & RIPE IP search)
IP Location: UK(UNITED KINGDOM)
Record Type: Domain Name
Server Type: Apache 2
Lock Status: clientDeleteProhibited
Web Site Status: Active
DMOZ no listings
Y! Directory: see listings
Secure: No
E-commerce: Yes
Traffic Ranking: Not available

Search

SEARCH AGAIN

Enter a search term:

e.g. networksolutions.com

Search by:
- (•) Domain Name
- ( ) NIC Handle

Data as of: 14-Jun-2005

○ **IP Address**

Search

Need to get your business online?
Our professional designers can build a custom Web site for your business.
$11.95/month, plus a $499.00 design fee

GO

PerformanceClicks™ from Network Solutions
Create and manage your pay per click advertising from as low as **$125/month** plus **$99 one time set-up fee**

GO

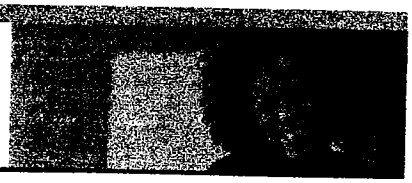
100% Secure Transaction
For your protection, this Web site is secured with the highest level of SSL Certificate encryption.

NetworkSolutions

Login

Customer Service
Call us toll free

Your cart is empty



WHOIS Search Results

Available **opc-agaricus** extensions:

.com	.org	.us	.mobi	.info	.biz	.de	.tv	.co.uk	.eu	.bz
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Order Selected Domain(s) >

Your WHOIS Search Results

IMAGE NOT AVAILABLE

opc-agaricus.net
Services from Network Solutions:

Certified Offer Service - Let us help you get this domain name!
Backorder - Try to get this name when it becomes available.
SSL Certificates - Get peace of mind with a secure certificate.
Enhanced Business Listing - Promote your business to millions of viewers for only $1 a month!

Please note: the owner of the domain name is specified in the "registrant" field.

In most cases, the Registrar is not the owner of domain names listed in this database.

Registrant:
William Isely
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States

Registered through: Cheap-DomainRegistration.com
Domain Name: OPC-AGARICUS.NET
Created on: 02-Jun-06
Expires on: 02-Jun-08
Last Updated on: 09-Mar-07

Administrative Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
(828) 369-7590 Fax --

Technical Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
(828) 369-7590 Fax --

Domain servers in listed order:
DNS1.SUPREMECENTER20.COM
DNS2.SUPREMECENTER20.COM

The previous information has been obtained either directly from the registrant or a registrar of the domain name other than Network Solutions. Network Solutions, therefore, does not guarantee its accuracy or completeness.

Show underlying registry data for this record

Current Registrar: WILD WEST DOMAINS, INC.
IP Address: 209.25.170.23 (ARIN & RIPE IP search)
IP Location: UK(UNITED KINGDOM)
Record Type: Domain Name
Server Type: Apache 2
Lock Status: clientDeleteProhibited
Web Site Status: Active
DMOZ no listings
Y! Directory: see listings
Secure: No
E-commerce: No
Traffic Ranking: Not available

Search

SEARCH AGAIN

Enter a search term:

e.g. networksolutions.com

Search by:
- (•) Domain Name
- ( ) NIC Handle

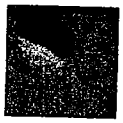
Data as of: 14-Jun-2005

○ IP Address

Search >

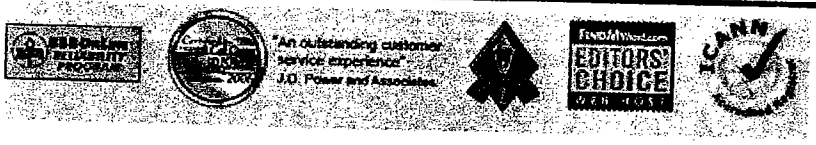
Need to get your business online?
Our professional designers can build a custom Web site for your business.
$11.95/month, plus a $499.00 design fee

Go >



PerformanceClicks™ from Network Solutions
Create and manage your pay per click advertising from as low as **$125/month** plus **$99 one time set-up fee**

Go >



100% Secure Transaction
For your protection, this Web site is secured with the highest level of SSL Certificate encryption.

ATTACHMENT C

ATTACHMENT D

Agaricus Net

Best Price/Best Quality

Agaricus blazei Murill from Brazil

Prostate Cancer Survivor

Over the years we receive a lot of questions from people about their health, particularly from men between 50 and 80 years old who are suffering from prostate cancer.

This is the story of Bill Isely who came to us in the summer of 2000, looking for a natural way to handle the prostate cancer his doctor had told him he had. He had an elevated PSA and problems getting up frequently at night. His doctor wanted to insert radioactive needles into his prostate. Instead he bought our RF 1000 and in a short time his PSA came down and his prostate problems went away. He took the AMAS blood test that showed his cancer was gone.

Now he helps other people get our products for their cancer problems like breast, lung, liver, and all the other cancer problems in this modern world of so much pollution. He is even working with doctors who want to use our latest miracle from the Rain Forest, the RAAX11.

He is in North Carolina and wants to help you. **Call 828-369-7590** to talk to him, or go to our home page and click on USA.

- Cancer
  - Breast Cancer
  - Leukemia
  - Liver
  - Lung Cancer
  - Prostate Cancer
- Discount
- HIV Treatment
- Shopping Cart/Sales
- Research
- Wholesales
- Products
- RAAX11
- Sales USA
- Testemonials
- Home

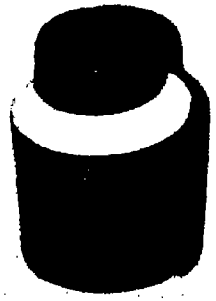
Agaricus Net

The only natural source for Agaricus blazei Murill (Agaricus brasiliense) from Brazil

International Sales - Europe - USA - Asia - Australia

Index Page

Discount
HIV Experience
OPC Agaricus
Testemonials
RAAX11
Research
Shopping Cart
Wholesales
Home
E-mail



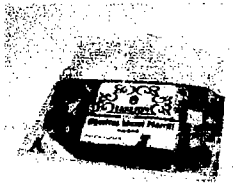
Original Natural Products from the brazilian Rainforest

Payments by PayPal

Agaricus Net German:: Store

Phone Order **866-944-7359**

Shopping cart for USA & Asia. (not for Europe)

Item		Quantity	Product Description	Unit Price
Agaricus dried Grade A 100gr bag		Quantity [ ] Add to Basket	Agaricus blazei Murill mushrooms have been know for their beneficial effects on the immune system since their discovery in the rain forests of Brazil by Mr. Takto-shi Furumoto about 35 years ago. By having tests made in Japan he confirmed what the residents of Piedade already had known for centuries.	**19.90 $**
Agaricus dried Grade A powder 100g bag		Quantity [ ] Add to Basket	We also supply the Agaricus blazei mushroom in bulk powder from which a tea is made. First the powder is soaked in cold water which is poured off and then the mushroom is boiled in new water. The two waters are combined to make the tea.	**24.90$**
Agaricus Capsules 500		Quantity [ ] Add to Basket	Agaricus capsules are often taken like vitamins as a means of strengthening the immune system due to the Beta Glucan that is in the Agaricus mushroom. Our capsules contain pure Agaricus powder of the Golden Quality with 60 capsules per bottle in two sizes, 500mg caps. Most of our competitors use low quality mushrooms in their capsules of grade B or C.	**19,90$**
Agaricus sweet Extract		Quantity [ ] Add to Basket	For conditions requiring the strongest Agaricus, the normal extract of Agaricus is used since it takes approximately 456 g of mushrooms to make a 100ml bottle of extract. To make it easier to take we offer it now with natural Stevia sweetener.	~~49,00$~~ **29.90 $**

FTC-00137

100ml bottle				
Agaricus strong Extract 100ml bottle		Quantity [ ]	For conditions requiring the strongest Agaricus, the normal extract of Agaricus is used since it takes approximately 456 g of mushrooms to make a 100ml bottle of extract. This product is mainly used for prevention of the immune system.	~~49,90$~~ **39.90$**
RF 1000 Extract 100ml bottle		Quantity [ ]	It is a special combination of Agaricus, Cats claw and Pau d'Arco Comes with a bottle of 100ml water extract. The strong extract shows the best results in many cases of immune system diseases and is used by natural doctors.	~~49,90$~~ **39,90$**
APM Extract 100ml bottle		Quantity [ ]	For some other conditions it is desirable to use the rain forest herbal combination which is Agaricus, Pau de Arco and Mutamba. This is called APM extract. Same like RF 1000 but for those people who can´t intake the Cats Claw, take this product.	~~49,90$~~ **39.90$**
RAAX11 Extract 100ml bottle		Quantity [ ]	Agaricus blazei Murill, RAAX11 ™ strongest juice extract, 1 x 100ml bottle, natural manufactured. **Mainly used to help to build up the immune system very fast. Ingredients are Icao plum and Agaricus blazei Murill mushrooms. Both are showing good results.**	~~329.90$~~ **149.90$**
OPC Extract 500ml bottle		Quantity [ ]	For some other conditions it is desirable to use the rain forest herbal combination which is Agaricus, Pau de Arco, Nerium Oleander & Cats Claw. Bottle with 500ml. Stronges Agaricus extract to build up very fast your immune system. Last at normal usage arround 200 days. The strongest for special treatments.	~~249,90$~~ **149.90$**
Camu		Quantity [ ]	Camu Camu extract capsules are natural vitamin C extracted from the reainforest bush, commonly known as Bilberry.	~~14,00$~~

FTC-00138

Camu 60 capsules		[redacted]	**9.90$**
Power Builder 60 Caps per bottle		Quantity [ ] [redacted]	**Power Builder capsules are a blend of rain forest herbs which are designed to provide vitality and energy in times when those apsects of our nature are run down due the stresses of modern living. Power Builder capsules contain Catuaba extract, Marapuama extract, Pfaffia, Maca and Tribulus Terratris extract. Normally used by people to get more power during some kind of medical treatments.**	~~15,00$~~ **9.90$**

I authorize to charge my credit card for the total amount of above order. I further affirm that the name and personal information provided on this form are true and correct. I understand that credit card fraud will be prosecuted to the fullest extent of the law. Your results may vary. Offer void where prohibited. US returning policy:

You may return most new, unopened items sold and fulfilled one of our wholesales within 2 days of delivery for a 90% refund. Items that are opened will not receive any refund.

Note: By pressing the ORDER Confirmations button below, I agree to pay.

[redacted]

Agaricus Net

Best Price/Best Quality

Payments by PayPal

Thank you very much we will contact you within 24hrs. In the meantime you may check our special prices for cancer patients.

Special Cancer Discount = choose the products you need - price in Euro

hidden="" type="hidden">

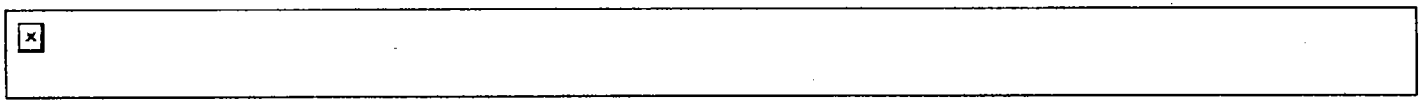
- Cancer
- Breast Cancer
- Cancer Form
- Leukemia
- Liver
- Lung Cancer
- Prostate Cancer
- Discount
- HIV Treatment
- Shopping Cart/Sales
- Research
- Wholesales
- Products
- RAAX11
- Sales USA
- Sales from Brazil NEW
- Testemonials
- Verkauf Deutschland
- Vendas Brasil
- Ventas Espana
- Vendas Portugal
- Investors
- Home

Item		Quantity	Product Description	Unit Price
RAAX11 special extract bottle with 100ml **The original one**		Quantity	Agaricus blazei Murill, RAAX11 ™ strongest juice extract, 1 x **100ml** bottle, natural manufactured.**Special Price**	**99.00€**
OPC Extract bottle with 500ml !!! The original one		Quantity	**For some other conditions it is desirable to use the rain forest herbal combination which is Agaricus, Pau de Arco, Nerium Oleander & Cats Claw. This is called OPC extract and registered at the Ministry of Health in South Africa, used their by many, many people, with a lot of sucess. Again the amount of usage might vary from one teaspoons to 5 per day. A advise of your doctor or health practitioner should be taken. It is often advantageous to take the extracts in combination with other Agaricus products like RAAX11.**	**99.00€**

I authorize Takesun USA to charge my credit card for the total amount of above order. I further affirm that the name and personal information provided on this form are true and correct. I understand that credit card fraud will be prosecuted to the fullest extent of the law. Your results may vary. Offer void where prohibited.

Note: By pressing the ORDER Confirmations button below, I agree to pay Takesun Portugal Lda.

FTC-00140



ATTACHMENT E

ATTACHMENT E

LIGGINS DECLARATION
CAPTURED WEBSITE WWW.AGARICUS.NET
DISC
DATED JANUARY 3, 2008

ATTACHMENT F

Agaricus Net

Best Price/Best Quality

Agaricus blazei Murill from Brazil

- Cancer
  - Breast Cancer
  - Leukemia
  - Liver
  - Lung Cancer
  - Prostate Cancer
- Discount
- HIV Treatment
- Shopping Cart/Sales
- Research
- Wholesales
- Products
- RAAX11
- Sales USA
- Testemonials
- Home

Prostate Cancer Survivor

Over the years we receive a lot of questions from people about their health, particularly from men between 50 and 80 years old who are suffering from prostate cancer.

This is the story of Bill Isely who came to us in the summer of 2000, looking for a natural way to handle the prostate cancer his doctor had told him he had. He had an elevated PSA and problems getting up frequently at night. His doctor wanted to insert radioactive needles into his prostate. Instead he bought our RF 1000 and in a short time his PSA came down and his prostate problems went away. He took the AMAS blood test that showed his cancer was gone.

Now he helps other people get our products for their cancer problems like breast, lung, liver, and all the other cancer problems in this modern world of so much pollution. He is even working with doctors who want to use our latest miracle from the Rain Forest, the RAAX11.

He is in North Carolina and wants to help you. **Call 828-369-7590** to talk to him, or go to our home page and click on USA.

Agaricus Net

Best Price/Best Quality

- Cancer
- Breast Cancer
- Cancer Form
- Leukemia
- Liver
- Lung Cancer
- Prostate Cancer
- Chemo Therapy
- **Cancer research**
- HIV Treatment
- Shopping Cart/Sales
- Research
- Wholesales
- Products
- RAAX11
- Testemonials
- Home

Agaricus blazei Murill from Brazil

Statistic for People who are using the RAAX11/OPC Agaricus protocol
Dr. Steven Hall reports that 100% of his patients are in remission. (16.08.2006)

This is the bad result if you are choosing Chemotherapy

Side Effects of Chemotherapy:
All drugs can have side-effects (unwanted effects). It is important to ask your doctor or nurse about the potential risks (side-effects) and benefits associated with your chemotherapy. This is important because each drug can have slightly different types of side-effects.

There are common side-effects associated with many chemotherapy drugs. Since these reactions may or may not be associated with your chemotherapy, you may want to ask if they will apply to your case.

A partial list of side effects includes: allergies, bone marrow depression, hair loss, mouth and throat problems, nausea and vomiting, sexual and reproductive problems, and skin changes.

Allergic Reactions:
Allergic reactions can occur after taking almost any drug (including chemotherapy). They can occur immediately or can be delayed. If severe, the drug will be discontinued. If mild, allergy treatments - e.g. suppression agents (typically more drugs) can be used to proceed with chemotherapy.

Common allergic symptoms include:
Rashes on the skin
Swelling
Shortness of breath
Rapid heart beat

Rare allergic symptoms include:
Decreased blood pressure
Shock
Kidney failure
Since most chemotherapy is given in a clinic or hospital, patients are typically watched for reactions after drugs are administered. In these controlled environments, prompt treatment is administered and allergic reactions are treated.

When at home after treatment, patients can notice late allergic reactions. If you notice skin rashes, weakness while standing or sitting, progressive swelling or any unusual changes you should contact your physician immediately.

Bone Marrow Suppression:
Bone marrow depression (suppression) is a side effect caused by certain

chemotherapy drugs. When it occurs, it typically happens 7-10 days after the chemotherapy is started and usually recovers after 3 weeks. There are biotherapy medications that can speed bone marrow recovery.

Blood cells and other blood components are made in the bone marrow. Therefore, bone marrow depression results in decreased numbers of white blood cells, red blood cells, and platelets.

When the body loses white blood cells (leukopenia), it is a greater risk for infection. When the body loses red blood cells (anemia), it can be associated with fatigue. When the body loses platelets (thrombocytopenia), the blood has trouble clotting and the patient is at greater risk for bruising and bleeding.

Symptoms suggestive of bone marrow depression?
Fever or chills
Fatigue
Bruising or Bleeding
If you have fever, chills, fatigue, bruising or bleeding call your doctor immediately. In most cases your physician can give you medicines to treat bone marrow depression. These drugs can treat infections and compensate for low levels of white blood cells, red blood cells, and platelets.

Hair loss - Alopecia:
Hair loss (alopecia) is a common side effect of chemotherapy, but not all chemotherapy drugs cause hair loss.

Not all hair loss is total. It can affect the head or all parts of the body. It can be gradual. Typically hair loss does not happen immediately. It starts several weeks after the first chemotherapy, then hair can thin or come out in clumps. Some people also experience scalp sensitivity.

It makes sense to use a mild shampoo, a soft hair brush, and low heat when drying your hair. Avoid dyes, perms and hair relaxers. In general, a short hair cut looks fuller. If you don't cover your head, you may need to use sun screen on your scalp.

It is normal to feel angry or depressed when you lose your hair. You should speak with your doctor or nurse about your feelings. There may be a support group or mental health professional who can help you. But remember, hair loss is usually a temporary side-effect. The hair will grow back.

Hats and Wigs:
Most sources say you should shop for a wig before you lose most of your hair. That way you can match your usual style and hair color. Consider getting a wig with tape-tab materials called "stickies." This will allow you to comb and style the wig without worrying about sliding. Most sources also suggest you buy two wigs so you can have one on while the other is being cleaned.

Check to see if your insurance company will cover its cost. If not, it is a tax-deductible expense (keep your receipt). Have the establishment write, "hair prosthesis as prescribed by doctor" on the receipt.

When buying a hat, make sure it will block the sun from hitting your scalp. Women also prefer to wear hats or turbans when at home. Don't forget your sunglasses.

Nausea and Vomiting:
Nausea and vomiting are the body's defenses against eating too much and its mechanism to get rid of toxic food and poisons. During vomiting, the muscles that normally push food down the gastrointestinal tract, reverse direction and send back the partially digested material.

Nausea and vomiting may occur within the first hour of chemotherapy and can last up to a week. Most of the time nausea goes away shortly after these drugs are given.

In severe cases, anti-nausea medications may be necessary.
That is because the vomiting patient may lose too much fluid and necessary minerals. When a patient is at risk of dehydration and blood chemical (electrolyte) imbalance, your doctor or nurse can prescribe medication to help you prevent or lessen nausea.

Other causes of nausea that cancer patients may be experience include stress, radiation of the brain, and anesthetics (associated with surgery).

Treatment of Nausea and Vomiting:
The primary treatment for nausea is anti-nausea drugs. Since they work best taken before chemotherapy, discuss this with your doctor before your next treatment (particularly if you were nauseated after your last treatment).

Other methods include: acupressure wrist bands which are available at most drug stores, fasting (do not eat) for a couple of hours before your treatment, try to keep your eyes open, and slowly deep-breathing through your nose.

If you are already nauseated from chemotherapy, do not eat a large meal or drink carbonated beverages. You may try to eat crackers, pretzels, or dry toast. Avoid foods with a lot of residue, salads, high fiber cereals or fatty and fried foods.

Sometimes, right after chemotherapy patients are only able to suck on ice chips, sip ice water, or mild herbal tea. Once patients are feeling better, they may benefit from chicken soup.

If nausea and vomiting persist, call your doctor. Some patients need to receive intravenous (IV) fluids and electrolytes (minerals).

Sex and Reproduction:
Chemotherapy-related sexual and reproductive problems can occur in both men and women.

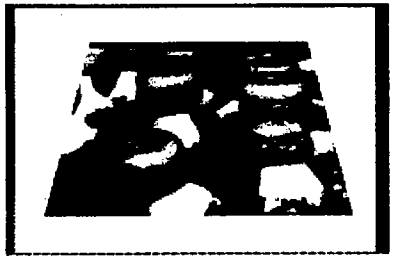
Since certain chemotherapy drugs may have harmful effects on an unborn child, genetic counseling should be made available to the chemotherapy patient in order to discuss the effects of drug therapy on current and future pregnancies.

References
1. Wilson MW, Czechonska G, Finger PT, Rausen A, Hooper ME, Haik BG. Chemotherapy for Eye Cancer Survey of Ophthalmology 45:416-444; 2001.

2. Calabresi P, Chabner BA. Chemotherapy of Neoplastic Diseases: Introduction. In: Goodman and Gilman's: The Pharmacological Basis of Therapeutics. Tenth Edition Hardman JG, Limbird LE, Gilman AG (eds.) McGraw-Hill, New York, 2001, Section IX, pp.1381-1388.

3. Chabner BA, Ryan DP, Paz-Ares L, Garcia-Carbonero R, Calabresi P. Antineoplastic Agents. In: Goodman and Gilman's: The Pharmacological Basis of Therapeutics. Tenth Edition Hardman JG, Limbird LE, Gilman AG (eds.) McGraw-Hill, New York, 2001, Chapter 52, pp.1389-1460.

ATTACHMENT G



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Dried ABM
Capsules
Extracts
Immune Kits
Contact

Our Agaricus

The Agaricus blazei Murill mushrooms from Brazil

Organic Agaricus Plantation in Brazil

RAAX11 bottle 100ml
$229
A i Murill andChrysobalanus Icaco Juice.
Used to build up your immune system.
Usage from 2,5 ml to 30ml per day.
100ml bottle at a special price

Order | View Cart

larger image

RF1000 bottle 100ml
$29.00 Special Price
A strong blend of Agaricus, Cats claw and Pau d'Arco to build up your immune system.

Order | View Cart

Agaricus blazei Murill Extract bottle with 100ml
$35.00
For conditions requiring the strongest Agaricus, the normal extract of Agaricus is used since it takes approximately 456 g of mushrooms to make a

Agaricus blazei Murill sweet Extract bottle with 100ml
~~$39.90~~ now $ 29.90
For conditions requiring the strongest Agaricus, the normal extract of Agaricus is used since it

FTC-00170

100ml bottle of extract.

Order View Cart

takes approximately 456 g of mushrooms to make a 100ml bottle of extract. To make it easier to take we offer it now with natural Stevia sweetener.

Order View Cart

The raw material

All our Agaricus extracts are made out of Grade A Agaricus blazei Murill mushrooms from Brazil. We use only the best quality. If you are interested in wholesales please contact us.

APM Agaricus extract - bottle with 100ml

$45.00

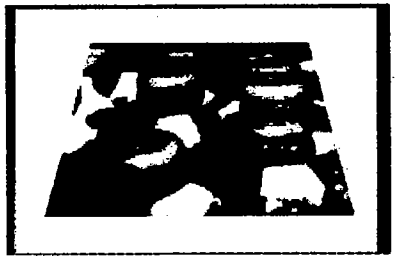
For some other conditions it is desirable to use the rain forest herbal combination which is Agaricus, Pau de Arco and Mutamba. This is called APM extract.

Order View Cart

I authorize to charge my credit card for the total amount of above order. I furthe affirm that the name and personal information provided on this form are true and correct. I understand that credit card fraud will be prosecuted to the fullest extent of the law. Your results may vary. Offer void where prohibited. US returning policy

You may return most new, unopened items sold and fulfilled by Gemtronics withir 2 days of delivery for a 90% refund. Items that are opened will not receive any refund.

Note: By pressing the ORDER Confirmations button below, I agree to pay Gemtronics, 28734, NC, USA



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Our Agaricus

The Agaricus blazei Murill mushrooms from Brazil

Organic Agaricus Plantation in Brazil

[redacted]

For more information or to order from us, select the product of your interest by clicking at left or right.
Or contact us by phone, FAX or email.

Bill Isely
-- Intl. Tel.xx1 828-369-7590
-- US Tel. (free) 866-944-7359
-- FAX. 828-369-5861
-- email

FTC-00175

ATTACHMENT H

Takesun do Brasil

- Home
- Company
- Contact
- International Agents
  - Austria/Germany
  - China/Hong Kong/Macau
  - Portugal/Spain
  - Singapore
  - South Africa
  - USA/Canada/Mexico
- Products
- Wholesales

Natural Food Suplements from Brazil

FDA registered Warehouse Franklin/USA

Looking for distributors - contact us for details -

Telephone 866 944 7359

China - Canada - Germany - Hong Kong - Macau - Portugal - Singapore - South Africa - Spain - Thailand - Taiwan - USA

Natural Food Suplements from Brazil

FDA registered Warehouse Franklin/USA

Looking for distributors - contact us for details -

Telephone 866 944 7359

ATTACHMENT I

From: service@paypal.com (service@paypal.com)
To: Riece Miles
Date: Thursday, January 3, 2008 1:08:19 PM
Subject: Receipt for Your Payment to gotto@takesun.com

PayPal *The way to send and receive money online*

Dear Riece Miles,

This email confirms that you have paid (gotto@takesun.com) $134.90 USD using PayPal.

This credit card transaction will appear on your bill as "PAYPAL".

Payment Details

Transaction ID:	20U8900657657914S
Item Price:	$134.90 USD
Total:	$134.90 USD
Order Description:	11263984: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90
Item/Product Number:	11263984
Invoice ID:	11263984
Buyer:	Riece Miles

It may take a few moments for this transaction to appear in the Recent Activity list on your Account Overview.

Business Information

Business:

Your Confirmed Address

Shipping Info: Riece Miles

Lorton, VA 22079
United States

If you have questions about the shipping and tracking of your purchased item or service, please contact at gotto@takesun.com.

If your email program has problems with hypertext links, then you may also confirm your email address by logging into your PayPal account at www.paypal.com/us. On your My Account page you will find a "Confirm Your Email Address" link. Click on this link and enter the following confirmation

number:

0653-8336-0122-8007-4430

Thank you for using PayPal!
The PayPal Team

Your monthly account statement is available anytime; just log in to your account at https://www.paypal.com/us/HISTORY. To correct any errors, please contact us through our Help Center at https://www.paypal.com/us/HELP.

FOR INTERNATIONAL PAYMENTS ONLY

Commissions and Fees incurred by sender: $0.00

Rate of Exchange: The above exchange rate includes a 2.5% spread above the wholesale exchange rate at which PayPal obtains foreign currency, and the spread is retained by PayPal. If and when the Recipient chooses to withdraw these funds from the PayPal System, and if the withdrawal involves a currency conversion, the Recipient will convert the funds at the applicable currency exchange rate at the time of the withdrawal, and the Recipient may incur a withdrawal fee.

RIGHT TO REFUND
You, the customer, are entitled to a refund of the money to be transmitted as a result of this agreement if PayPal does not forward the money received from you within 10 days of the date of its receipt, or does not give instructions committing an equivalent amount of money to the person designated by you within 10 days of the date of the receipt of the funds from you unless otherwise instructed by you.

If your instructions as to when the money shall be forwarded or transmitted are not complied with, and the money has not yet been forwarded or transmitted, you have a right to a refund of your money.

If you want a refund, you must mail or deliver your written request to PayPal at P.O. Box 45950, Omaha, NE 68145-0950. If you do not receive your refund, you may be entitled to your money back plus a penalty of up to $1,000.00 USD and attorney's fees pursuant to Section 1810.5 of the California Financial Code.

Important Note: The Right to Refund claim process applies only to payments that have not been successfully transmitted to the recipient. With PayPal, almost all payments are transmitted to the recipient immediately, except for eCheck payments, and payments to non-PayPal members.

Please do not file a Right to Refund claim if your payment has already been completed. If you have problems with a completed payment or need assistance with settling a dispute with a seller, go to PayPal's Resolution Center by logging into your account and clicking the Resolution Center sub tab located at the top center of the Account Overview page.

You can also click the Help link at the top right of any PayPal page to look up more information about the Resolution Center and filing complaints.

MA residents only: PayPal holds a Foreign Transmittal Agency license in the State of Massachusetts - License Number FT3345.

Please do not reply to this email. This mailbox is not monitored and you will not receive a response. For assistance, log in to your PayPal account and choose the Help link located in the top right corner of any PayPal page.

To receive email notifications in plain text instead of HTML, update your preferences here.

PayPal Email ID PP120

gotto@takesun.com

Receipt

PayPal Secure Payments

Ship To: Riece Miles

Lorton, VA 22079
United States

Seller Information: gotto@takesun.com

Transaction ID: 20U8900657657914S

Placed on Jan. 3, 2008

Payment For	Quantity	Price
11263984: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90 Item #11263984	1	$134.90 USD

Subtotal:	$134.90 USD
Sales Tax:	$0.00 USD
Total Amount:	**$134.90 USD**

Print Done

PayPal. The safer, easier way to pay.
For more information, read our User Agreement and Privacy Policy.

Schedule package pickup right from your home or office at usps.com/pickup

Print postage online - Go to usps.com/postageonline

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1300 0001 3103 1332

DOMESTIC ONLY

3103 1332

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28734
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AMOUNT

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TM

From:/Expéditeur:

William Isely
964 Walnut Creek Rd
Franklin, NC 28734-9533

To:/Destinataire:

Riece Miles

Lorton, VA, 22079

Country of Destination:/Pays de destination:

required return address
addressee information in customer
block area or on label.

Payment Method
Affix postage or meter
indicated in upper

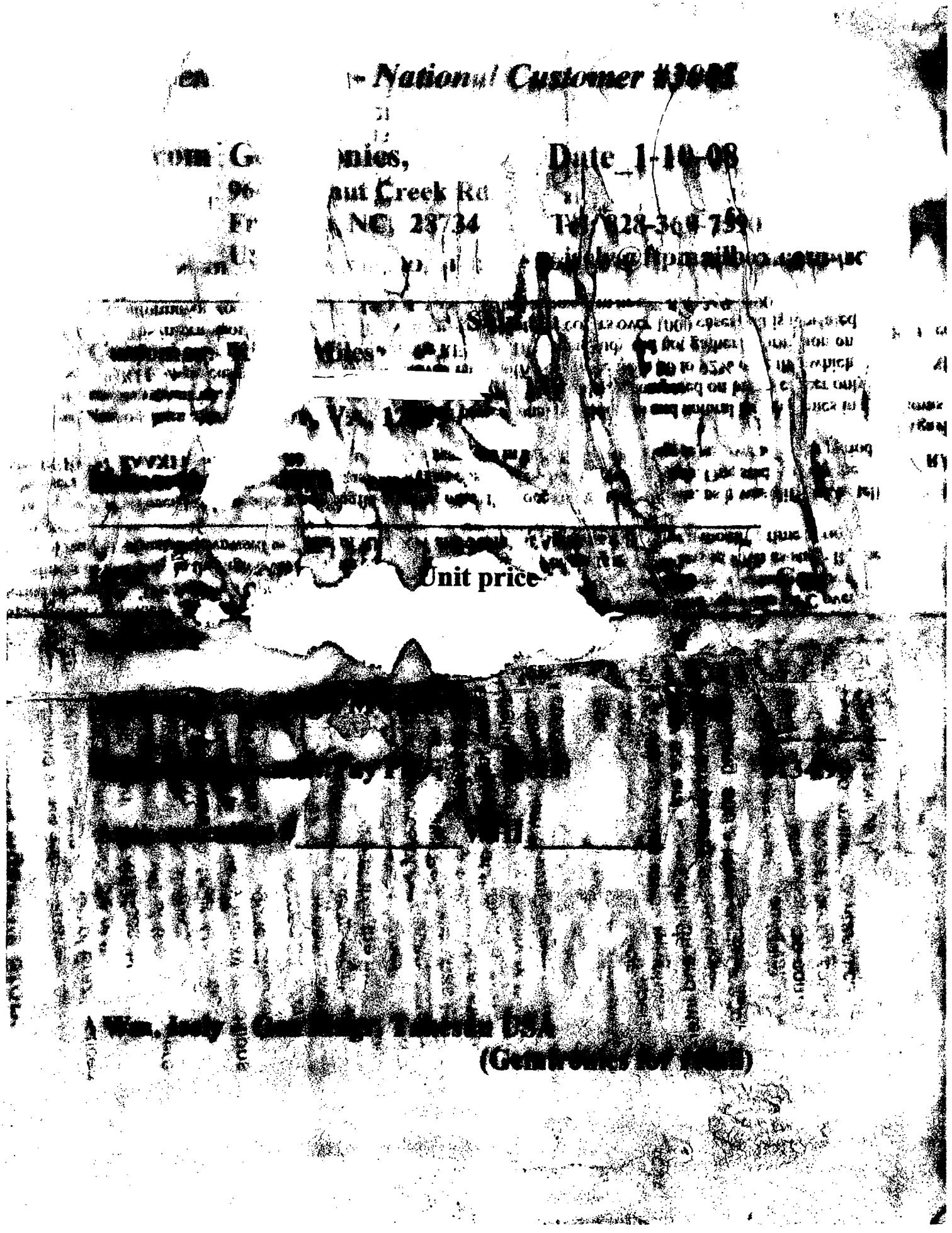
☒ LIQUID
☐ FRAGILE
☐ PERISHABLE

to schedule
paid envelopes
.com/pickup.

cradletocradle
SILVER

Cradle to Cradle Certification is awarded to products that pursue an **innovative** vision of **ecologically-intelligent design that eliminates the concept** of waste. **This USPS® packaging has been certified for its material** content, **recyclability, and manufacturing characteristics.**

enclosed, as long as the envelope is not modified, and the contents
with the adhesive provided as the means of closure.


National Customer
Date 1-10-08
Unit price

ATTACHMENT J

Takesun do Brasil

Verifiy that you are in following countries: USA, Canada, Australia or Asia. Other countries will be delivered through other agents. Look into your country page. (EU-Distributors: Austria, Germany, Portugal, Spain)or contact sales@agaricus.net

Product	Quantity	Price	Amount
Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original	1	119.90	119.90

	Subtotal	119.90
All prices are in US Dollars	**Shipping**	15.00
	TOTAL	134.90

US customers: UPS ground: 5 business days, UPS air: 3 business day delivery. International customers only Asia & Australia. Europe enter in your country page: EMS shipping arrives within 5-10 working days, Global Priority Mail 10 to 18 days.

Billing details

Dana Long

Roanoke, VA 24018
United States
Tel : 703-532-
Fax :
dana_long@yahoo.com

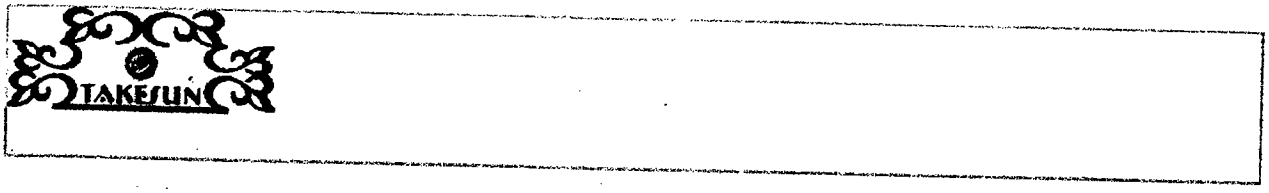
Shipping address (if different from the billing address)

Payment options

◉ Credit card or direct cash payment via **PayPal**

CONTINUE

Your Credit Card is charged using a SSL secured server. On your statement will apear GEMTRONICS SECURE PAYMENTS



Review Your Payment

PayPal Secure Payments

Review the payment details below and click Pay to complete your secure payment. Visit Funding Sources to learn more about PayPal policies and your payment source rights and remedies, or to change debit card processing options.

Item	Unit Price	Qty	Total
11306829: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90 Item # 11306829	$134.90	1	$134.90

Add special instructions for the Merchant

Enter Gift Certificate, Coupon, or Reward

Subtotal: $134.90
Total: $134.90 USD

Pay $134.90 Now

Payment Method:

Credit Card : Visa XXXX-XXXX-XXXX-6891 $134.90 USD

This credit card transaction will appear on your bill as "TAKESUNPORT".

Change

Shipping Address:

Dana Long

Roanoke, VA 24018
United States
Change

Contact Information:

dana_long@
703-532-
(Takesun Portugal Lda. Verkauf Deutschland requires a phone number to complete this order.)

Change Phone

Pay $134.90 Now

PayPal. The safer, easier way to pay.
For more information, read our User Agreement and Privacy Policy.

From: service@paypal.com (service@paypal.com)
To: Dana Long
Date: Wednesday, January 23, 2008 11:27:52 AM
Subject: Receipt for Your Payment to Takesun Portugal Lda. Verkauf Deutschland

PayPal *The way to send and receive money online*

Dear Dana Long,

This email confirms that you have paid Takesun Portugal Lda. Verkauf Deutschland (vendas@takesunportugal.com) $134.90 USD using PayPal.

This credit card transaction will appear on your bill as "PAYPAL *TAKESUNPORT".

Payment Details

Transaction ID:	00061355NC651964H
Item Price:	$134.90 USD
Total:	$134.90 USD
Order Description:	11306829: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90
Item/Product Number:	11306829
Invoice ID:	11306829
Buyer:	Dana Long
Phone:	703-532-

It may take a few moments for this transaction to appear in the Recent Activity list on your Account Overview.

Business Information

Business:	Takesun Portugal Lda. Verkauf Deutschland
Contact E-Mail:	vendas@takesunportugal.com

Your Unconfirmed Address

Shipping Info:	Dana Long Roanoke, VA 24018 United States

If you have questions about the shipping and tracking of your purchased item or service, please contact Takesun Portugal Lda. Verkauf Deutschland at vendas@takesunportugal.com.

Thank you for using PayPal!
The PayPal Team

Your monthly account statement is available anytime; just log in to your account at https://www.paypal.com/us/HISTORY. To correct any errors, please contact us through our Help Center at https://www.paypal.com/us/HELP.

FOR INTERNATIONAL PAYMENTS ONLY

Commissions and Fees incurred by sender: $0.00

Rate of Exchange: The above exchange rate includes a 2.5% spread above the wholesale exchange rate at which PayPal obtains foreign currency, and the spread is retained by PayPal. If and when the Recipient chooses to withdraw these funds from the PayPal System, and if the withdrawal involves a currency conversion, the Recipient will convert the funds at the applicable currency exchange rate at the time of the withdrawal, and the Recipient may incur a withdrawal fee.

RIGHT TO REFUND
You, the customer, are entitled to a refund of the money to be transmitted as a result of this agreement if PayPal does not forward the money received from you within 10 days of the date of its receipt, or does not give instructions committing an equivalent amount of money to the person designated by you within 10 days of the date of the receipt of the funds from you unless otherwise instructed by you.

If your instructions as to when the money shall be forwarded or transmitted are not complied with, and the money has not yet been forwarded or transmitted, you have a right to a refund of your money.

If you want a refund, you must mail or deliver your written request to PayPal at P.O. Box 45950, Omaha, NE 68145-0950. If you do not receive your refund, you may be entitled to your money back plus a penalty of up to $1,000.00 USD and attorney's fees pursuant to Section 1810.5 of the California Financial Code.

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Please do not file a Right to Refund claim if your payment has already been completed. If you have problems with a completed payment or need assistance with settling a dispute with a seller, go to PayPal's Resolution Center by logging into your account and clicking the Resolution Center sub tab located at the top center of the Account Overview page.

You can also click the Help link at the top right of any PayPal page to look up more information about the Resolution Center and filing complaints.

MA residents only: PayPal holds a Foreign Transmittal Agency license in the State of Massachusetts - License Number FT3345.

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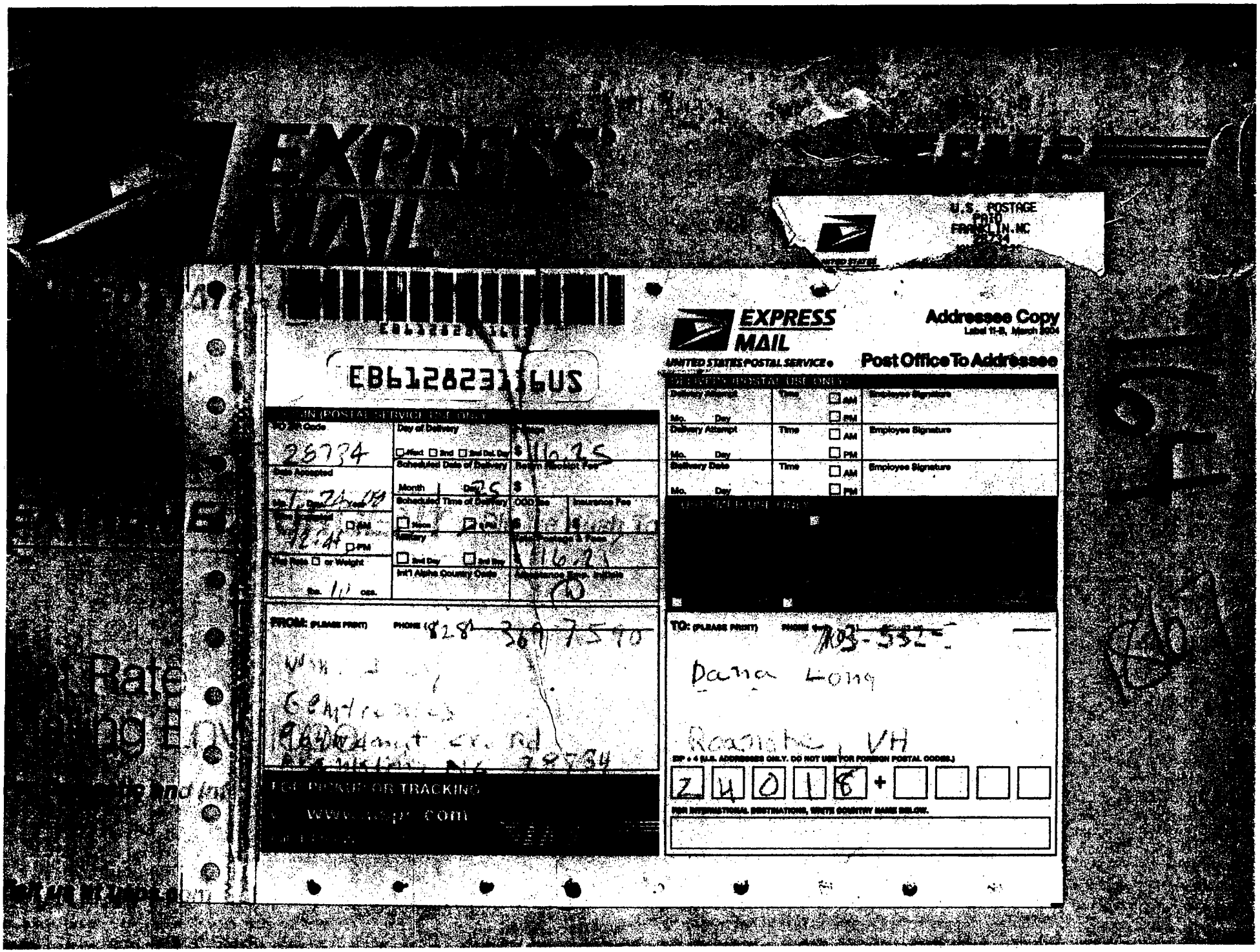
To receive email notifications in plain text instead of HTML, update your preferences here.

PayPal Email ID PP120


EXPRESS MAIL
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PAID
FRANKLIN, NC
EB612823116US
EXPRESS MAIL
Addressee Copy
UNITED STATES POSTAL SERVICE
Post Office To Addressee
FOR POSTAL USE ONLY
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Flat Rate
Scheduled Time of Delivery
Insurance Fee
Flat Rate ☐ or Weight
lbs. 1 oz.
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PHONE (828) 369-7570
TO: (PLEASE PRINT)
PHONE (703) 352-
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Roanoke, VA
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24018
FOR INTERNATIONAL DESTINATIONS, WRITE COUNTRY NAME BELOW.
FOR PICKUP OR TRACKING
www.usps.com


Shake well before usage
SUGGESTED USAGE
As an herbal dietary supplement, take 2.5 ml in tea or water 1 - 3 times daily. Our Chrysobalanus Icaco Agaricus juice extract is produced in Brazil. It is concentrated to enhance the benefits of the mushroom juice extract and is produced using international standards and with 100% Quality Control. All Takesumi herbs are naturally produced in Brazil.
TAKESUMI
RAAX11
Strong Water Extract
A Dietary Supplement
Net 100 ml
Supplement Facts
Amount Per Serving
Chrysobalanus
Agaricus blazei
FDA Product Code

Shipment Invoice - National Customer #3019

From Gemtronics, **Date_1-24-08**

964 Walnut Creek Rd.
Franklin, NC, 28734 **Tel: 828-369-7590**
USA **w.isely@ftpmailbox.com**

Ship to:

Customer: Dana Long

Roanoke, VA, 24018

Phone:703-532- **email:**

Item	Unit price	No	Cost
RAAX11	$119	1	$119
Method Of Ship: UPS	shipping & Handling	Cost:	15
Method of payment: Pay Pal		Total	$134

Authentication #_____WHI_____

Note: Please order direct by phone or email in the future.

Thanks, Bill Isely

OPC
500ml - new

Camu Camu
120 Caps $15

The Agaricus blazei Murill Mushrooms are grown in their natural location free of any contaminants, dried so as to conserve their important nutrients of which Beta Glucan is critical for strengthening the immune system.

Takesun do Brasil

Then packages the mushrooms in various ways: dried, powder, extracts, capsules, and also in combination with other rain forest herbs for exporting to many countries around the world.

For more information go to web site:

Go to www.agaricus.net
Click on USA sales. or
www.our--agaricus.com

Gemtronics
Tel: 828-369-7590
Email:w.isely@ftpmailbox.com

The Agaricus Story

Some years ago a Japanese researcher In the Piedade section of Brazil noticed that the native people of the rain forest who used the Agaricus blazei Murill mushrooms as part of their diet were much healthier than the westerners who ate a conventional diet. He noticed that they were particularly free of conditions that we today call degenerative ones.

Samples of the mushrooms were sent to Japan where the mushrooms were seen to have beneficial effects which were attributed to the fact that the mushrooms were found to have the highest known natural source of beta glucan, among other nutrients. Beta glucan has long been known as a substance that stimulates killer cells of the immune system, cells very critical to the ability of the immune system to handle degenerative conditions.

Agaricus blazei Murill mushrooms were found to have other beneficial properties as well. Besides immune enhancing, they are anti-tumor, interferon and interleukin enhancing, anti-viral, cholesterol reducing, and a blood sugar modulator.

Agaricus has also been found valuable for certain conditions when combined with other rain forest herbs: cat's claw, pau d'arco, mutamba,. camu camu, and Chrysobalanus Icaco.

TAKESUN® U.S.A.

Agaricus Mushroom Products From The Rain Forest

FTC-00024

--- POPULAR PRODUCTS ---

Agaricus Blazei Murill Mushrooms 100 g, Grade A $25 Golden $29.90

Normally packed in an air-tight bag for long-term preservation, the mushrooms can be soaked and cooked before eating or just soaked and cooked and the water then poured off to drink as a tea for therapeutic purposes.

The active constituents are Beta Glucan (1-3-3 glucan) and Ergoaterol (rovitamin D2) derivatives.

Agaricus blazei Murill Powder

100 gram bag

For those making large quantities of tea, mainly for therapeutic purposes, the mushroom powder is available as the most economical form to take the Agaricus mushroom. For best results, Agaricus should be taken with about 6,000 mg of vitamin C every day, which can be in the form of Camu Camu. For good health it is also recommended to keep the body on the alkaline side.

Agaricus Blazei Murill Capsules $12

60 Capsules, 500 mg.

The capsules are commonly used for preventative purposes, similarly to taking vitamins. Usually several capsules are opened into a cup of hot water to make a tea.

Extracts For Therapy Purposes

Agaricus and blends of it with other rain forest herbs in the extract form are what are usually used for therapy purposes.

Agaricus Blazei$ 25 Murill Extract

100 ml.

Many Westerners consider the making of the tea each day to be an inconvenience and prefer to take their Agaricus in the form of an extract. A 25:1 extract Is available so that the tea can be made by adding 5 ml (1 teaspoon) of the extract to a cup of water or other drink.

Depending on their status, people who take the extract for therapy reasons may use up to ten bottles of it in a month. For preventative purposes, people normally will use one bottle a month.

RAAX11

An extract Blend of Chrysobalanus Icaco & Agaricus - 100 ml

$119

For some conditions, the Agaricus works best when it is combined with other herbs. The RF 1000 is a combination with Cat's Claw and Pau d'Arco. .

RF 1000 Extract

100 ml. **$25**

As with the Agaricus powder, a liquid extract is available in the RF 1000 for those who prefer to use the liquid to make a tea.

APM JUICE

100 ml. **$25**

A version of the RF 1000 extract is available in which the Cats Claw has been replaced with the herb Mutamba which is better for some conditions.

FTC-00025

RAAX11 / AGARICUS OPC PROTOCOL DESCRIPTION AND RESULTS

Takesun has been developing various Amazon Rain Forest derived liquid extract blends, all involving the Agaricus brazei Murill mushroom, principally for support of combating various degenerative health conditions. The RAAX11 / Agaricus OPC protocol for stage IV conditions is the taking of 500ml of RAAX11 and 1000ml Agaricus OPC over a period of a month. The Agaricus OPC part is gradually introduced over a period of a month to six weeks to allow the adjustment of the body to the high level of waste elimination that results. For cases at lower levels, such as stage II, the protocol may be adjusted downward to 300ml of RAAX11 and 500ml of Agaricus OPC over a month's time period.

In the past it has been hard to collect meaningful results, other than occasional testimonials, as it was difficult to tell if the users followed the protocols and in most cases were not observed by health professionals. One study, using the older RF1000 / RAAX11 protocol, yielded a successful response in 80% of breast cancer cases over a 1 year period.

Takesun has now been able to gather meaningful data from professional practitioners and natural health clinics in a number of European countries, Germany, the UK, Austria, and Spain. The results, if compared on breast cancer only, are that the RAAX11 / Agaricus OPC protocol has improved the positive response from 80 to 92% over that which was demonstrated by the older protocol, RAAX11 with the RF1000. The older study did not gather information on other conditions. The information on the RAAX11 / Agaricus OPC protocol covers over 1000 cases and is tabulated below. For more information contact William H. Isely at w.isely@ftpmailbox.com or call 828-369-7590.

CONDITION	No. OF CASES	No. RESPONDING	% RESPONDING	% NOT RESPONDING
Lung	413	321	78	22
Gastro	122	99	81	19
Intestinal	55	35	64	36
Larynx	21	9	43	57
Esophagus	25	13	52	48
Brain	29	21	72	28
Lymphatic	5	3	60	40
Breast	371	342	92	8
Leukemia	41	32	78	22
Sarcoma	4	3	75	25
Thyroid	5	4	80	20
Prostate	76	65	86	14

While the lifestyles of these individuals are not known, it is assumed that they represented a cross-section of Europeans. Someone on the protocol also going onto a Mediterranean diet, avoiding most meat, using organic sources as well as using good supplements, including anti-oxidents, could reasonably expect an even better outcome.

RAAX11 - 100ml

(Agaricus and Chrysobalanus Icaco)

$119 Each

Protocol - 5 bottles/month

Agaricus OPC - 500ml

(Agaricus, Nerium Oleander, Pau d'Arco, and Cat's Claw)

$130 Each

Protocol - 2 bottles/month

FTC-00026

COMPLAINT COUNSEL'S EXHIBIT 3

I N D E X

E X H I B I T S

Complaint Exhibits
Marked for Identification

Respondent's Exhibits
Marked for Identification

UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

In the Matter of:

GEMTRONICS, INC., a corporation, and

WILLIAM H. ISELY, Individually and as the Owner of Gemtronics, Inc.

DOCKET NO. 9330

Wednesday, February 4, 2009

Oakhill Country Inn

1689 Old Murphy Road

Franklin, North Carolina 28734

The above-entitled matter came on for deposition, pursuant to notice, at 10:20 a.m.

Reported by:

Mary K. Huth-Stepp, Registered Professional Reporter

A P P E A R A N C E S

On Behalf of the Federal Trade Commission:

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MS. BOLTON: This is the deposition of William H. Isely in the matter of Gemtronics, Inc., et al., FTC Docket No. 9330. My name is Barbara Bolton and I'm complaint counsel for the Federal Trade Commission. And at this time I'd ask the other counsel to state his appearance for the record.

MR. VAN HORN: My name is Matthew I. Van Horn and I'm counsel for both respondents Gemtronics, Inc. and individually, William H. Isely.

WILLIAM H. ISELY,

a witness, called for examination, having been first duly sworn, was examined and testified as follows:

EXAMINATION

BY MS. BOLTON:

Q. Good morning, Mr. Isely. Thank you for being here today. Have you ever had your deposition taken before?

A. You mean in this case or in some other --

Q. In another case. Have you had a deposition before?

A. I don't recognize it. I think not.

Q. All right. I'll be taking your deposition today. And the court reporter will be recording your answers. Since this will be a written transcript, it is important that you answer questions verbally and not use

gestures or nods and the like because it cannot be recorded accurately by the court reporter.

If you do not understand a question that I ask you, please let me know. I'll be happy to rephrase it for you. If you do understand a question, I'll assume -- I'm sorry. If you do answer a question, I'll assume that you did understand it.

If you would like to speak with your attorney during the deposition, that's fine. I would just ask that if there is a question pending, please conclude your answer before conferring with counsel.

If you would like to take a break for any reason, bathroom break, you want a glass of water, you want to stretch, that would be fine and I would be happy to accommodate you.

Is there any reason why you cannot testify truthfully and accurately to any questions that I pose to you today?

A. Well, I can't answer that until I know what the questions are.

Q. But it's your intent to answer?

A. None that I know of. None that I assume you would ask.

Q. Are you experiencing any medical condition that may affect your ability to recall or testify truthfully

today?

A. Well, I'm just getting old and memory is not as good as it used to be.

Q. And are you presently taking any medication that would affect your ability to recall or testify truthfully?

A. I don't think so.

Q. I'll begin by asking you to tell me a little bit about yourself. For the record, can you state your name and address?

A. William H. Isely. 964 Walnut Creek Road, Franklin, North Carolina, 28734.

Q. And can you tell me a little bit about your background. For instance, can you tell me about your education?

A. Well, I was born in Turkey in 1925. My parents were missionaries. And I was home schooled till high school. Well, I guess I had one year back in the United States when I was 10 years old. And then I went to Beirut Community, American Community School for two years. And then before the war I came back on a trans steamer, lived with my grandmother in Kansas, where I finished up my high school.

Well, during the last part of high school the war started and so without a break from high school, I

went to college. I went to Carnegie Tech to start with. And then I was classified to be drafted and there was a period of time where I did part-time jobs. And then I got a job in an aircraft factory, waiting to get drafted. It didn't seem to happen, so I went back to school at Northwestern for a year.

And then I did get drafted. And it was strange. I was drafted into the Navy, which is unheard of. Because the Navy was usually filled up with volunteers. They had more people to try to go to the Navy to avoid the Army, but there towards the end of the war everybody wanted out, so the Navy had to draft people, too. So I spent some time in China as a radio operator.

Q. Did you get a college degree?

A. Yes. After the war I came back and went to -- continued at Northwestern under the GI bill and I got a BS in mechanical engineering and --

Q. And what year did you get that?

A. Well, actually, I finished school in 1948, but it was -- I had to go to summer school to finish up, the way it worked out. And so I think on my records they show it as '49, the class of '49. But actually I started working in '48 with Westinghouse.

Q. And did you get a graduate degree at all?

A. Yes. They sent me to graduate school, which

from my point of view was a very cheap way of doing it. So I got a master's in electrical/mechanical combined.

Q. And where did you get that from?

A. University of Pittsburgh, which is where I was working for Westinghouse.

Q. And then after college, why don't you just tell me your employment history briefly.

A. Well, we -- I was in, you might say, the defense industry. We were making turrets and other equipment for airplanes. You know, the ball turrets that they put in the tails of the bombers and making computers for those, and I was involved in that. And I got involved in some of the early missiles.

Q. And who did you work for, when you did that?

A. This is for Westinghouse.

Q. For Westinghouse. All right. And then how long did you work for Westinghouse?

A. Well, let's see. '48 to about '55.

Q. Okay. Then who did you work for after?

A. Part of that time I moved to another facility they had, which was in Baltimore. They set up a special division to work on airplane problems. But I was trying to get them interested in space, and they said, oh, there's nothing that ever happened to that. They wouldn't spend any money on it, so I changed jobs. I

went to work for Boeing.

Q. And that was in '55?

A. '55. And they started me out as an engineer in charge of testing a missile that Boeing was developing at that time called the Boemark. And it was a fighter missile without a pilot. Take off like a rocket and then get up to 60,000 feet and then it would look for the bombers it was supposed to shoot down. Kind of an interesting project.

Q. And how long did you work for Boeing?

A. Two years.

Q. And then you went to where?

A. Well, I was going to go to work for Martin, but I got an offer from Honeywell, first, over in St. Petersburg. And they were in the aerospace business as well. So I guess they thought they needed what I -- my expertise and so I was there for 33 years, worked on a number of missiles and rockets and also one spacecraft.

And my highest position was program manager of a program that probably took in, over the life of the program, two billion dollars in defense-related business. That was a guidance system for the rocket that -- well, we probably, probably built 155 of them. I think they are still building them, as a matter of fact.

Q. And did you retire from Honeywell?

A. I retired from Honeywell.

Q. What year did you retire?

A. I think it was '87. My retirement was kind of intermittent. I did some consulting part time for a while with them, but mostly I was -- I think I came up here in summer of '87.

Q. And have you been employed since your retirement?

A. I had two consulting, very short consulting jobs. One was with an Italian aerospace company, the reason I got to go to Italy to do that. But other than my self-employment, the answer is no.

Q. And what have you been doing then for self-employment?

A. Well, this goes back to '71. I was having some health problems, just didn't have much energy and I consulted with some M.D.s. Couldn't get any help. They said, well, you're 45 years old, you've got to slow down. Well, I wasn't ready to.

And I talked to some nutritionists and we came up with I was getting too much animal fat, which was probably clogging my arteries, as people experience these days. You hear it on television. So they recommended I go on a vegetarian diet, and I did that.

And the first six months was real tough. I

thought it was a mistake. But what happened was I didn't study nutrition well enough to know that a vegetarian has got to eat differently. I just stopped eating meat and fish and eggs and chicken, but I didn't think about where was I going to get my protein. So after I adjusted that, I had to study nutrition to find out what was best for me. And my health got a lot better. And I said, hey, this is good stuff.

I was telling some of my friends. And they were -- and they didn't want to bother. Most of the things were available in the common health food stores, don't have to mail away for them, like Spirulina, methionine. Well, microhydrin turned out to be a very good product. These were sort of cutting-age products that hadn't yet gotten into the mainstream market.

And so my friends would ask me, well, gee, we don't want to bother, but could you sell us a bottle? Pretty soon I found I had a little business going. And I specialized more in Dr. Hill's products. He was -- Dr. Christopher Hill, he's no longer alive. But Royal Body took over his products.

There were some ingenious things he came up with, based on studying why the HuntSA people lived so long. And it turns out it is the minerals in their glacial water they drink. He studied how to synthesize

the same minerals.

Anyway, I made a little business of it. When I retired, I continued it.

Q. Did you sell under any particular name or were you just selling informally?

A. Well, I was just -- I was just selling under my own name. And then when I got up here and started some local sales, I realized I needed sales tax certificate and to collect sales tax.

Down in Florida, the products weren't under sales tax and so I hadn't been involved in that so much. And at the time I needed to -- I was also interested in rocks and gems. So I thought a name to connect some of the interests I had that represented that, I called it Gemtronics. And that's the name that I registered in, I think it was '93, with the state, as a -- let's see what my category is. Mail order, basically mail order and it was largely dietary supplements. And I picked up a couple other brands, Mannatech brands of products.

And what really happens is, I was watching for new things that would come out. And because one of my principles was if everybody is doing it, it's like there's another Chinese tailor down the corner and you can't charge more than he does. And so I was always looking for things that hadn't gotten widespread

distribution.

When something got saturated, I probably would start moving into something else. And let's see, how we got into --

Q. Were you selling -- as part of your nutritional supplement business, were you always doing business out of your home?

A. Yes.

Q. All right. So you didn't have any, any --

A. I didn't have an office.

Q. -- business location?

A. No. Originally it was by mail and then my son introduced me to computers. And kind of hard to say, early 1990s I think I had my first computer that ran on DOS rather than -- it was before Windows. I made up a chart that shows -- I'd like to pass this out.

MR. VAN HORN: It was the Exhibit A to our interrogatory responses.

MS. BOLTON: Uh-huh (affirmative).

MR. VAN HORN: I've provided her with that.

THE WITNESS: It will help if you have it while I talk, because my business got more complex as I got picking up Takesun products.

BY MS. BOLTON:

Q. All right. So, according to your chart, it says

you added Takesun, you started adding Takesun products to those you sold in 2000?

A. How about -- see, I had a neck surgery in late 1990s. And they discovered that while I was in the hospital I had enlarged prostate. And they had me get on a screening program. And I had a rather -- a level of PSA for some time and then one year it spiked up from 9 to 16 in a short period of time, and my doctor suggested I see a urologist. And he did a biopsy and found I had prostate cancer. And his solution was to load me up with radioactive pellets. And I asked him, well, what's the long-term result of that. And he said, well, it's too new. We don't know yet, but we think it's a good thing to do.

I had reservations about -- I have had about radiation for a long time. Particularly in Florida, when they started radiating tomatoes and all variety of other things. I wasn't sure that was good for me. So I started researching what natural -- well, my Doctor said, your rate of increase is not too bad. You can wait a while and see what you want to do, rather than go into a sudden surgery.

So I looked naturally on what was available on the Web, I tried a number of things. I eventually ran across Agaricus Blazei Murill, which is a technical name

for the mushroom that Takesun sells. And it was available from a couple of medical people, but they were basically buying for their patients. And they would quite often be out or they wouldn't have enough to spare for me, so -- and my PSA was coming down rather quickly, so I was quite interested in it. So I started buying it directly from Brazil.

Q. And what was the company name that you purchased from?

A. Takesun do Brasil. It's a Portugese spelling of Takesun of Brazil.

MR. VAN HORN: It's D-O?

THE WITNESS: It's D-O, then B-R-A-S-I-L. Then my point of contact was George Otto Kather, who was a German born, immigrated to Brazil. And my understanding is he married a Brazilian lady and set up his business there.

Q. Is he the president of Takesun do Brasil?

A. I have no idea what his official duties are. It seemed to be sort of a family-owned business. And I don't know. It is called LDA. I don't know if that's like limited in this country or what. They have that after the name, LDA.

Q. But as far as you know, does George Otto Kather run Takesun do Brasil?

A. As far as I know, he appears to be the main person, yes.

Q. Okay.

A. And because he's multi-lingual, he deals with the international business. He speaks German, Portugese, Spanish, and probably in order of proficiency English. His English is pretty bad, but he -- he gets along with it.

Q. And you started buying Agaricus products from Mr. Kather?

A. Well, from Takesun.

Q. From Takesun do Brasil?

A. Yes.

Q. And that was in 2000 you started that?

A. I would say early 2000 I was buying it basically retail and some of -- I had quite a lot of customers by that time buying other products. A lot of them was interested in anything new I came up with. So it looked like it was something to add to my business.

So I needed a name and I came up with Nature First as the name. And that's what I imported under after I started more than just for myself.

Q. And was that a registered company or was that a d/b/a or what kind of --

A. No, it was just a/k/a, if you want.

Q. It was a name you did business under?

A. Yeah.

Q. Okay. And then when did you start using Gemtronics with regard to purchasing Agaricus products?

A. Not yet. What happened shortly after that was that one of my main buyers is a lady, Jane X, out in the West Coast, asked to be a partner in my importing business. She wanted to import to the West Coast and customers she had. So we formed a legal partnership. And I've given you the federal ID we registered under. And it was actually from probably around June of 2001 until December.

And we originally planned -- we divided the business. I was going to continue handling the importing, she was going to be the warehouse and both of us had retail business, but she was going to ship out all our retail sales and maintain the stock in her place. We got halfway through that transition and she just didn't like the business. She didn't think it was making as much money as she thought it ought to and so we closed out the partnership that year.

In other words, we had -- December 31st we reported the taxes for the year we had been in business and closed it out. And that was Takesun, U.S.A.

Q. That was the name of your partnership was

Takesun, U.S.A.

A. Yes.

Q. Okay. And was that a registered partnership?

A. Well, it had a Federal ID. I guess to that extent it was registered.

Q. Okay. Now, after the dissolution of your partnership, did you continue doing business under the name Takesun, U.S.A.

A. Well, I had to close out the bank account and so on, but within a few months I made no more purchases. I transferred the stock, we divided up the stock. And as far as any business went, we were done by December of 2001.

Q. And after --

A. Now, I left the name on my -- I left the name on my, what's the word, my brochure, in the event that somebody else would want to be under, at least under my importing of -- I wanted to keep my importing name. I wanted to keep that as a potential importing name, if I went back into that mode that I had been with Jane, but that never happened.

Q. So Takesun, U.S.A. was a name that you used to import product?

A. Yes.

Q. So you imported Agaricus products?

A. Yes.

Q. And were these Agaricus products imported from Takesun do Brasil?

A. Yes. And then I went back to using Nature First as my importing company, let's say, in 2002. And I switched over to selling from Gemtronics, which was -- because Gemtronics had the retail registration and retail tax collection capability that Nature First did not.

Q. Oh, so let me just be clear. So Nature First is a name that you used in starting in 2002 for importing products from Takesun do Brasil?

A. No, I started -- no, I went back to that.

Q. But, I mean, you began using it again?

A. I started using it again.

Q. Now, did you have an importing license to import these products?

A. At some point I registered with the FDA and I have a registered approval, what they called an approved warehouse. This means that they have vetted your business background and so on and are a legitimate business, not, you know, somebody that's laundering money or something else. And it makes -- it helps the FDA in the customs aspect because of -- they can just go to the file and pull up anything they want, any information on you they want, without having to get it on every import.

And I was importing as often sometimes as once a month, so that's -- and then, of course, Homeland Security came in and put in their rules of prior notice. Where anything, any importing has to have a prior notice form filled out and filed with the FDA. And that turned out to be a fiasco because they wanted you to identify the flight and the time within an hour of when your shipment was going to arrive. Well, with international flights and weather, it turned out that three quarters of the time it came on a different airplane at different times and you were supposed to let them know. Well, the logistics of that just was difficult.

Q. All right. Now, let me clarify. So you have an FDA approved warehouse, correct, for importation?

A. I listed my house, right.

Q. And you imported product from Takesun do Brasil. Did you import any other products?

A. No.

Q. So you were the exclusive -- that was exclusively Takesun products that you imported?

A. Uh-huh (affirmative).

Q. Okay.

A. But I was not exclusive with Takesun.

Q. Takesun -- in other words, did Takesun -- were there other people in the United States or businesses in

the United States --

A. Oh, yes.

Q. -- that you knew that imported Takesun products?

Oh, yes. See, I was -- Takesun, I was importing enough volume that Takesun offered me an exclusive if I would sign up as a dealer. There were many reasons I didn't. For one thing, he offered me a contract which I would call written in pidgeon English. And George learns his English by hearing it. I don't think he ever had any official schooling. So two words that sound the same, he would use them interchangeably.

Q. So you had no distributorship, formal distributorship agreement?

A. No. Every purchase was a stand-alone, separately negotiated on price, on how it was to be sent and, you know, whether it was to be sent express or with one of the freight companies, and when it would be delivered. So that made it a little more difficult because I had been a distributor.

But I was concerned about his advertising and I became more concerned, I think, in about '62, about the time I had moved, moved out of the partnership.

MR. VAN HORN: 1962?

THE WITNESS: No, no, '92. '92. No, 2002. Go back to my chart and I won't forget. I think he told me

in an e-mail that FDA had been on his Website and told him they didn't like it or anyway there was some complaint to him. And he investigated it, and he told me that he didn't come under the FDA or the United States jurisdiction, so it wasn't a problem for him.

I recognized it might be a problem for me to have any formal ties with, any legal ties with Takesun, so I strictly avoided that.

Q. All right. So then all you did was buy product from him or import product from Takesun; is that correct?

A. Well, Takesun -- as an inducement to buy from him, Takesun had offered a free Web service. And at the time I was with Nature First, the way he did that was you went to an address at .net.

Q. What year now are we talking about?

A. Talking about -- years, I'd say 2001, 2002. You went to Agaricus.net and you clicked on U.S. sales, and that, that clicked over to my Web pages.

Q. And Agaricus -- tell us what Agaricus.net is.

A. Agaricus.net is the main Website for the Agaricus products that is owned and controlled by Takesun do Brasil. And so I got concerned that I was going through Agaricus.net to get to my pages. Actually, they weren't my pages in the sense that I was -- I never learned how to run a Website, but I would, I would say

what -- I would get the material in the way of general terms of what I wanted and we'd spend several interactions getting right English on it, you know, and making sure that this is on my pages of Nature First.

Q. All right. So Nature First had a Website; is that what you're saying?

A. No, they had pages. There's a difference.

Q. They had Web pages?

A. Web pages on Agaricus.net. And about 2002 --

MR. VAN HORN: Do we want to have him say what those Web pages are? Are they -- is it just a page or is it actual, like a Website?

MS. BOLTON: He just said it wasn't a Website.

MR. VAN HORN: It's just a page.

THE WITNESS: Well, it was pages. In other words, it was a subset of about four pages that you could -- when you clicked the U.S. sales on Agaricus.net, you went to what was my home page, and then there were several other things you could click to.

Q. So if you were on the Website of Agaricus.net and you wanted to buy product, Takesun products in the U.S., you would click on the U.S. sales whatever button and it would go to your Web pages; is that correct?

A. Uh-huh (affirmative).

Q. Okay. And those were, again, those were your --

you had registered Web pages or they were not registered?

A. Registered with whom? Is it --

Q. Like a domain. You didn't have a domain?

A. No. A domain is only for a Website, like Agaricus.net. Now, if somebody was searching the net and put in the right words, they might end up with that page, but the normal way to get there would be from Agaricus.net.

Q. All right. So, in other words, is it your belief that you could not independently get to your Web pages, but actually you had to go through Agaricus.net to get to your Web pages?

A. No. If you were surfing on the net and put in, let's say, dried mushrooms, it could very well come up with one of my pages because the Web crawlers, they don't -- they will just look for the words that somebody has put in, regardless of how they get there, you know. But anyway --

Q. Let me clarify one thing. If you were on Agaricus.net, you said for U.S. sales, if you wanted U.S. sales, then it would go to you. Were you the sole contact through that Website for U.S. sales?

A. No. As a matter of fact, Jane X, she had pages there, too.

Q. So how would, how would -- if you clicked on

U.S. sales, how would it go to you or how would it go to Jane X?

A. Well, I think it went to a sub page, where you had a choice, you know. Her page or mine. And we anticipated others might want to be there, also, but it never happened.

Q. So there was initially two, two sellers that you could buy from in the United States?

A. No, you could -- there are other companies independent.

Q. I meant through Agaricus.net.

A. From Agaricus.net? No. If somebody went to Agaricus.net main shopping cart, they could buy from anyplace in the world.

Q. I'm talking about for U.S. sales.

A. For U.S. sales as well.

Q. And how long did that situation go on? I mean, did Jane X continue on in business at the same time that you did?

A. Yes, because she, she -- he left her Web page for her, even though she wasn't buying. She turned around and bought from me after that. She didn't want to import. But I think he left her page up for another six months. But at that time something happened where -- I don't know if his, George Otto's attention went

elsewhere, but he wasn't maintaining the pages. A lot of times they wouldn't work. I told him to forget it and took the link out. So I just stopped using that page that had been made, those pages that were made up for Nature First, probably in 2002.

Q. Okay. And what happened after 2002?

A. Well, I decided that I needed an independent Website. It would have its own address. And I looked at how to do it and I didn't have the time and energy to generate one. And George says, well, I can arrange for one for you. It would be independent, in terms of no links to his. And he registered in 2004, I think, in June, he registered two Websites for me. They were Our-Agaricus.com and .us. And one was a mirror image of the other. It just registered two so that gives you twice the possibility of getting hits, if you have more domains. So these were now domains on their own.

Q. And these were your domains; is that correct?

A. We got into an interesting definition of your. Actually, I wasn't -- his offer as part of buying products from him was to actually manage and control the -- even the domain. So I was still just suggesting what I wanted on there, but he was the actual one who registered it. I asked him to register it in my name, and he did, but he kept -- he managed it and controlled

it. He kept the PIN number, password and the account number. I never had those.

Q. All right. Were you -- but they were Agaricus.com and Agaricus.us? I'm sorry, Our-Agaricus.com and --

MR. VAN HORN: Is it Our dash?

A. Our dash.

Q. Our-Agaricus.com and Our-Agaricus.us, were those registered in your name?

A. Yes. But it turns out that registration means nothing in the -- I had a long conversation with the registrant company and I found out that I had been registered elsewhere. And they said, well, we don't ask for ID verification. People can put down whatever they want in the slots where the registrant, the technical manager, the administrative manager and the other one, I think, is the billing manager. He says, we don't -- he says, a lot of companies will put different names down, so it doesn't mean anything. He says, the person paying for the site gets control of it.

Q. All right. Let's talk about just -- let's go back to the Our-Agaricus.com and Our-Agaricus.us. You said they were registered in your name. Did you pay for those registrations?

A. No.

Q. No. Did you receive bills for those registrations? Annual bills to renew the registrations?

A. No. I got a notice and at the time it didn't mean anything to me. I don't know which registrant companies. There were quite a few registrant companies. And they try to take the rental fees away from each other. So they search the Website and find out domains that are about to come due for rental and they will send you a form that says, we would like to register these domains. This is not a bill. And I got one, I think it was in 2006. And it had some Websites on it that weren't mine, including mine. And I asked, by e-mail, I asked George Otto, I says, what's this all about? He says, don't worry about it. I take care of it. And that's the last I heard of it. So I figured it was some kind of mistake.

And if I really followed that up, I would have realized back in 2006 that he had registered some of his other Websites in my name, also. But none of those did he, did I have control, in terms of the tools it takes to manage and control the Website. He kept those.

And an interesting fact, and I'll be glad to share it with you, if you ever get involved in this kind of thing again, is that when this is done by e-mail, the e-mail of the person actually doing the transaction is

included in a WHOIS generally. And if you look at the WHOIS you got, you'll find that every one of them has one of George Otto's e-mail addresses. None of them have mine.

MR. VAN HORN: Can we just clarify that when you say look at the WHOIS, for what?

THE WITNESS: I've got that here.

Q. Well, let's not go there because I will introduce these later.

A. Well, I'd like to make my point to show you what I'm talking about, so when you look at it later you'll understand.

MS. BOLTON: Well, are you going to introduce these as exhibits? I mean --

MR. VAN HORN: Sure.

THE WITNESS: These are yours.

MS. BOLTON: I understand that. And I'm going to introduce them as exhibits. If you want to just talk about them briefly, that's --

MR. VAN HORN: Why don't you do this, why don't you not introduce this as an exhibit. Why don't you show her what the page is and so it will be a reminder when she introduces it, we can discuss it then.

THE WITNESS: Okay.

MS. BOLTON: And --

MR. VAN HORN: And we'll let her --

THE WITNESS: I want to make sure this is -- no, that's Our-Agaricus. That's mine. That's Takesun. Yeah, it's the one for Agaricus.net is on FTC 00162. And then the, yeah, and the e-mail that was --

MR. VAN HORN: Just show it to Barbara.

THE WITNESS: Oh, okay. The mail, only e-mails on there are George Otto, Takesun.com.

MR. VAN HORN: So the import of it, you're saying that's your name, but next to it is somebody else's --

THE WITNESS: Yeah.

MS. BOLTON: Okay. All right. Let's go back to -- when did you start --

MR. VAN HORN: Hold on. Did you want to say something?

THE WITNESS: Well, we were going over the history, which we didn't finish.

BY MS. BOLTON:

Q. I'd like to get to -- you were saying that you imported -- when did you start doing business under the name Gemtronics, in terms of using Nature First and start using the name Gemtronics?

A. Nature First was to import. I used Gemtronics as a sales tool for retail from the beginning of the time

that I picked up Takesun products.

Q. And that was about what year did you start using the name Gemtronics again?

A. I was using it all the time.

Q. How far back, would you say?

A. From the time I registered at North Carolina in 1993.

Q. Okay.

A. And, of course, I didn't have the Takesun as part of my offering until the year 2000.

Q. Now, at some point you incorporated Gemtronics?

A. Yes. Actually, just going down the history, RAAX started importation in 2004. I had my first sales of RAAX in 2004.

Q. All right. Let's, let's stop there for a minute. You're talking about the RAAX product?

A. RAAX product.

Q. And that's R-A-A-X11. It's actually RAAX11. We'll --

A. RAAX11.

Q. We'll call it RAAX.

MR. VAN HORN: And it's capitalized.

Q. You started importing RAAX in 2004?

A. Yes.

Q. Okay. Were you importing under the Gemtronics

name?

A. Yes. At that time I had consolidated all the business under Gemtronics, including -- I would say at the end of 2003, I was -- I had stopped probably even in 2002 the Nature First aspect. So I consolidated everything under Gemtronics, including the importing. Now --

Q. And you were using Gemtronics as a d/b/a at that time, as a doing business as?

A. Yes. Now, George never got used to my name changes and so he would sometimes send products to me personally. Sometimes they would be addressed to -- usually Nature First would be in there because that was what would have been registered with the FDA. So as far as George was concerned, it didn't matter, as long as he got paid.

Q. Now, what made you decide to start selling the RAAX product?

A. Well, there was interest in it. I mean, right now you go to the -- you go to Google, you put in RAAX11, and you'll get, I don't know, I think you'll get 480 hits. There was a lot of information on RAAX out there on the Website. And people asked for things that are coming out new and it sounds like an interesting product, so --

Q. And RAAX is made from -- is that an Agaricus product?

A. It's a combination of Agaricus, Blazei Murill and Chrysobalanus Icacco. And those are common names for both of those. One is called Agaricus, one is called cocoa-plum. Now, cocoa-plum, if you go to -- you'll get over, I think, two million hits on Google, if you go searching on cocoa-plum. You won't go so many on Chrysobalanus Icacco. That's a botanical name most people don't know.

Q. And how did you first learn about the product RAAX?

A. I believe in an e-mail from George who told me he had a new product that I might be interested in.

Q. And what made you decide to sell RAAX?

A. It was just another item in the line of things offered related to products I was already carrying.

Q. And how did you get your supply of RAAX?

A. Like I got everything else. I would negotiate a purchase with George and how many bags of mushrooms and how many containers of powder and how many bottles of capsules and how many bottles of Agaricus extract and how many bottles of RAAX. And he'd give me a price and sent it off sometimes in just one big box that would come apart on the way.

Q. And how did you sell RAAX to consumers? I mean, how did you advertise RAAX to consumers?

A. I just put it on my brochure.

Q. And when you, when you sold RAAX, you said you sold it through a brochure. How else did you sell it? How did you advertise that you sold this product besides just a brochure?

A. Well, see, I had made out a business strategy which is different from most people. And most of the people on the Web are trying to get as much money as they could. And that wasn't -- I felt that was being kind of greedy because most of the prices were at least 100 percent profit. And I looked at what the -- a decent profit and figured out that I have the lowest price on the Web, and I didn't need to advertise.

People would -- people on the Web, they go around, they may go to 10 different sites till they find the lowest price. And as long as it's the same thing, they buy it for the lowest price. So my strategy was not to advertise, other than just list it as being for sale on my Website and also on the brochures that I would send to my other customers who might be buying microhydrin or Mannatech products or spirulina.

Q. All right. So you sent brochures out to existing customers. And where were your existing

customers located? Were they located throughout the United States?

A. Throughout the United States, although predominant location was in California. There seemed to be a greater interest in natural products in California, the western states.

Q. And did you sell the RAAX product to consumers throughout the United States?

A. Yes.

Q. And you said you listed the product on your Website. Now, which Website are we referring to now?

A. Our-Agaricus.net. I mean, .com and .us.

Q. Okay. And did either of these Websites have links to other Websites?

A. No.

Q. All right. So you advertised by brochure and on the Website. Were there any other means you used to advertise RAAX?

A. No.

Q. Okay.

A. See, my philosophy was that I was retired, I had a retirement income. Rather, I wouldn't say meager, but just modest. And I was quite satisfied. I didn't want to work day and night. I got adequate sales just by having people find me on the Web, as well as customers

that I already had.

Q. Now, if a customer found you on the Web, how would they place an order with you via the Web?

A. Pardon me?

Q. How would a consumer who saw an advertisement on the Web, on a Website for RAAX, how would they order the product from you?

A. Almost always they would call because unless you're a very sophisticated business, you can't tell a person ahead of time what his shipping is going to cost. And he may want it overnight or he might be willing to have it next week. And because of the shipping issue, people almost always called me. And my telephone number was on the Agaricus, Our-Agaricus.com or, yeah, it's basically, if they found it there.

Actually, bulk of my customers were old customers and customers that were repeats. New customers were quite rare, as a matter of fact.

Q. And when customers called you, how would you know that they found your telephone number from a particular Website?

A. Usually they would tell you.

Q. And they would tell you -- did customers tell you that, I saw your phone number on Our-Agaricus.net?

A. If they didn't tell me, I could usually tell by

their questions. Because my Website was uniquely different from any others. So, you know, they would be asking me about this product, that product, and what I had said about it, which was generally just a list price. And Agaricus in general, I didn't put much more information on my Website.

Q. And --

A. Other than how the product was processed, so they would know that it was high-quality product.

Q. And did your phone number appear on other Websites that the -- other than Our-Agaricus.net and Our-Agaricus.us?

A. I had authorized -- George Otto asked if -- he used testimony, testimonials back in the beginning of our relationship. And he heard about my successful outcome on prostate cancer and he just wanted to have a testimonial. And I told him, well, my medical records are a fact that can be substantiated, if somebody has a question. And I'll give you a short summary of my medical records at best. And I prefer not to be identified by name, but I'll use my middle name. And I gave him a statement that he could use. And that was, that was all I authorized.

Q. Okay.

A. I subsequently, after your investigation,

discovered that he had used my name in other ways without my permission and without my knowledge.

Q. And what other ways was that?

A. As you pointed out, one was to call me to get information. It didn't say to call me to buy, because he was, he was selling -- during his last four years of this history I was telling you about, he was an active competitor of mine. Even though he was supplying me with product, he would, he would make more money if he could get the retail sale, rather than just the wholesale sale.

So he didn't say, call this number to buy, as I looked at it and as you have on your images of the Web pages that you've taken. I think, if I recall, it says, for more information call Bill Isely, and then there's a number.

And then the other thing I discovered, again, from you, is that he had used my name in renewing the registration of some of his domains.

Q. So when people called you to order RAAX product, you're not really sure whether they called you because your number was in your Website Our-Agaricus.net or whether your number appeared in one of Mr. Otto's Websites; is that correct?

A. As I told you, I would generally know from the conversation. And these calls are actually very rare

because particularly if they are international calls, I had some customers in Thailand, more of them in -- what's the Chinese island that broke away from the main land?

MR. VAN HORN: Japan?

THE WITNESS: No, not Japan. Taiwan. Yeah.

MR. VAN HORN: Taiwan.

A. And some from South Korea. People on the Internet don't like to use phones. And I think that was what Otto did. I don't know for what reason he put my name on there. I could speculate. But certainly wasn't successful. I can't remember a call and somebody said, I'm on Agaricus.net and your name is here and I'm calling you. People just don't call on the Internet anymore. It costs money to use a telephone, compared to sending an e-mail.

Q. But, in fact, you said that that's how you got your orders were from people calling you from your Website Our-Agaricus.net?

A. Well, I got -- I think I estimated for you in some material that you've been given that I got maybe two and a half percent of my calls that way. Or business, two and a half percent of my orders probably came in that way.

Q. So is it clear to say that you, when someone would call you, you really didn't know where they got

your number?

A. I wouldn't know in every case. In most cases I did.

Q. Now, when you fulfilled an order -- scratch that. Did you accept orders when -- when people ordered off -- they saw your name off the Web, did you have a PayPal account on your Website?

A. I did not accept PayPal. I do have a PayPal account where people can pay me, but it wasn't on my Website. I indicated, you know, if they called me, that they could pay with their credit card.

Q. All right. So you did accept credit card payments?

A. Uh-huh (affirmative).

Q. And I'm unclear about PayPal. Could people purchase product from you through PayPal?

A. No.

Q. Okay. And how -- when you fulfilled these orders, what -- if a consumer ordered RAAX from you, what would you send them? What would be in the package?

A. For an average customer, I would send the brochure.

Q. And by the brochure, you mean --

A. Well, the undercover agents that you had buy products got brochures, so you know what the brochure is.

It has about 10 products, a picture of it and prices associated with each product.

Q. And did you include invoices in your packages?

A. Invoices, yes.

MS. BOLTON: Okay. I'd like to take a break for a minute.

(Recess taken from 11:13 a.m. to 11:20 a.m.)

BY MS. BOLTON:

Q. Mr. Isely, are you still doing business under the name Gemtronics? Are you continuing to do business?

A. Gemtronics is out of business. Your publicity scared off most of my customers to the point where I was losing money and I stopped importing. And I've canceled my retail tax number.

Q. Are you continuing to sell any products?

A. I don't have any products. Well, this is -- I have this (indicating). I kept one.

Q. And by this, he's referring to a bottle of RAAX. He kept one.

MR. VAN HORN: Can I see that?

(Tendered).

Q. Okay. Mr. Isely, according to your Answers to Interrogatories, you sold approximately, from January 1st, 2004 to December 31st, 2008, 1,134 bottles of RAAX?

A. That's best as I can get from my records.

Q. Okay. And your sales were approximately about 115,000 for that, for those years?

A. Hmm?

Q. Your sales for 2004 through 2008 were about, approximately, $115,000?

A. On -- think I figured the average price is about 120, so I guess so.

MS. BOLTON: I'd like to have this exhibit marked as Exhibit 1.

(Complaint Deposition Exhibit No. 1 was marked for identification).

BY MS. BOLTON:

Q. Mr. Isely, I'd like you to look at that. And this also has Respondent's Bates number as 00006. Can you tell me what this is, Mr. Isely?

A. Well, it looks like a search report on a domain.

Q. And the domain is Our-Agaricus.com. And is this one of the Websites that you sold the product RAAX from?

A. Well, let's see. I'm trying to find the -- oh, yeah, this is Our-Agaricus.com. This is my Website. I said my Website. It's the Website that had my material on it.

Q. Okay. And did you register this domain name?

A. No.

Q. Okay. Even though you are -- it states that you are listed as the registrant?

A. That's what it says, but I didn't do it. You notice Agaricus, George Otto at Takesun.com has got his name associated with mine.

MR. VAN HORN: When you talk about a document, she has to write it down.

THE WITNESS: Oh.

MR. VAN HORN: So you kind of have to be more specific than normal.

THE WITNESS: Okay.

MR. VAN HORN: So if you walk through the document, identify, like there's the administrative contact.

Q. So the registrant is listed as William Isely?

MR. VAN HORN: On the far left side of the document.

A. That's what it says.

Q. And are you also listed as the administrative contact?

A. Administrative contact is William Isely and then it gives George Otto at Takesun.com as the address for me. Yeah. Which is, of course, incorrect, because that, that's for a Website located in Brazil. I've never been in Brazil since 1941.

Q. Now, did you -- but as you said, this was your domain. So you gave Mr. Otto permission to use your name in registering this domain?

A. Yes.

Q. And is this your -- under the administrative contact, the telephone number, 828-369-7590; is that your telephone number?

A. Yes.

Q. Okay.

A. I might mention, since I did business with George every month, he had all my contact information at hand. So the fact that my telephone number is on there doesn't mean that I put it there.

Q. But you did state previously that you allowed Mr. Otto to register this under your name?

A. Yeah. At the time I didn't know there was a difference between a registrant, an administrative contact, technical contact. And for some reason they didn't put the billing contact on there. That's usually a third name that for some reason it was omitted.

MR. VAN HORN: Flip the page, see if it's on the next page.

THE WITNESS: Hmm?

MR. VAN HORN: Flip the page, see if it's on the next page.

THE WITNESS: No, the next page is --

Q. And you said you had Web pages under the domain Our-Agaricus.com?

A. Up to the age -- year of 2002, at most.

Q. And after 2002, what happened?

A. They disappeared and I didn't have a link to them. And I don't know what happens to Web pages. I think they have a graveyard they go to somewhere after they are taken out of use, but I've never been there.

Q. Did you -- so is it your testimony that after 2002, this Website was no longer on the Web, up on the Web?

A. My pages on that Website. The Website was still there. Agaricus.net has been there since 1998.

Q. This is Agaricus.com.

A. Well, my Web pages that you're talking about were not -- this thing was created 2004. So that those pages that you're talking about were on Agaricus.net, not on Our-Agaricus.com. There was a two-year hiatus that I didn't have any pages anywhere.

Q. All right. I guess I'm not clear.

A. This one, this particular Website or domain was created in June of 2004. So you can't talk about it existing in 2002. It didn't. That was the other pages we talked about earlier, which were on Agaricus.net that

I no longer had use of after 2002.

Q. So did you -- so it's your testimony that as of 2004, you had no contact with this Website?

A. No, I say that's when it was created. George created it in June of 2004.

Q. Okay. As far as you're aware, did it have any information for you on this Website, any contact information for you?

A. Yes. It had my name, address and telephone number.

Q. And were you aware that your name, address and telephone number were on that, on the Website?

A. Yes. That's where -- that's how I expected people to contact me.

Q. And when customers placed orders through this Website for RAAX, how did they contact you?

A. Well, by calling.

Q. Do you know how many orders were placed for RAAX to you via Our-Agaricus.com?

A. I didn't keep records that way. No way I could tell you.

MS. BOLTON: All right. I would like to mark this as Exhibit 2.

(Complaint Deposition Exhibit No. 2 was marked for identification).

BY MS. BOLTON:

A. I did a sampling one time and I estimated about two-and-a-half percent of my orders, and they were almost always a sample type order, like one bottle or something like that that came off this Website.

Q. And how did you come to that figure?

A. I sampled a two-year period.

Q. And what two-year period was that?

A. Probably from May of 2008 going back two years, something like that. At one point in time you had asked for information that started and ended in May, and so I had made that sample, try to recreate how many orders I was getting from this Website.

Q. Mr. Isely, can you identify what this document is?

A. This is a WHOIS search results on the domain Agaricus.net. And it's kind of interesting, I notice that my name is misspelled, which I don't deliberately do.

Q. But you're noting that your name is listed as the registrant; is that correct?

A. Yes.

Q. And are you also the administrative, technical and zone contact?

A. Let's see. On the next page still misspelling

my name and giving my wrong telephone number. And the contact is given as e-mail address, gotto@takesun.com. And he also puts his name alongside mine. And I asked him about that one time.

Q. And when was that?

A. Hmm?

Q. When was that?

A. The spring of this year, where I was working pretty hard to get my name off of any of his material. I asked him about that. And he said, oh, I needed or I wanted to have an address in the United States. And he says, I only listed you as a contact point, I didn't put you down as a registrant. Well, I guess you have to get the experts on the registrant company to explain how they could put two names down in one place and get my telephone wrong and use George Otto's e-mail as to the point of contact.

Q. Mr. Isely, do you remember having a telephone conversation with me in March of 2008, after you received the Commission's --

A. Yes.

Q. -- proposed complaint?

MR. VAN HORN: Hold on. Don't interrupt. Let her finish, first of all. Second of all, you need to listen to that question closely.

THE WITNESS: Yeah, okay.

MR. VAN HORN: Because I'm just going to object to the extent you're stating evidence that's not in the record. You stated that after he received a letter from the FTC?

MS. BOLTON: No, I didn't say a letter from the FTC. I said, after he received our proposed complaint.

MR. VAN HORN: Okay.

Q. Do you recall receiving our proposed complaint package in March of 2008?

A. Yes.

Q. And did we have a telephone conversation on March 28th?

A. About that time. I couldn't -- you know, without looking at a calendar and my records, I couldn't be sure that was the date. But I think it's in that time period.

Q. And do you recall telling me during that telephone conversation that you had given Mr. Otto authorization for you to be a contact point for Agaricus.net?

A. No. I'm sure that at the time I was -- if I said anything like that, I was talking about Our-Agaricus.com. And I don't think you knew, at that time, that there were two Websites. And they sound very

similar to somebody who is just getting into it. I suspect that was a mistake you made.

Q. The complaint lists the Website Agaricus.net. It cites a complaint of Agaricus.net. So we were talking about Agaricus.net at the time because Our-Agaricus.com wasn't in the complaint.

A. I know it wasn't in the complaint, but it was in my conversation upon explaining it to you, as to what I had done and why you might be confusing me with George Otto.

Q. All right. And do you recall me asking you how it was that your name would have appeared on the domain registration for Agaricus.net, not Our-Agaricus.net?

A. I certainly gave -- I certainly wouldn't have told you that I gave him permission, when I didn't.

Q. Okay. So you did not give -- is it your testimony that you did not give Mr. Otto permission to use your name as a contact in the United States for the purposes of Agaricus.net?

A. No.

MR. VAN HORN: Did you understand that?

THE WITNESS: Well, it's a very general question. For the purposes of --

MR. VAN HORN: If you need her to specify and clarify, you know, you can ask her that. You don't want

to --

THE WITNESS: We were talking about registration and now you just broadened the question to any purpose. And maybe we could get back to a more specific question.

MR. VAN HORN: I think her question is fair, I just wanted to make sure you understood it.

Q. What -- why don't we say it this way. What permission did you give Mr. Otto in the sale of Agaricus products to use your name? When was he allowed to use your name and your address in the United States and your telephone number, to use your personal information for business purposes?

A. I never gave him permission to do that. Now, we've been talking about putting it on his Website. Are you expanding it beyond that?

Q. No, you said his Website. Is there -- you said that you allowed him to use your name and information on his Website. Were there any other instances where you allowed him to use your information?

A. The information about my cancer.

Q. No -- okay.

A. That was, at some point, if you want to know the recreation of the statement that I allowed him to use, we can put that into evidence. I don't know. Do you want to do that?

Q. Well, no. I mean, I don't -- we don't need to do that. That's fine. So you're saying then that to register Agaricus.net in your name as it's done here was done without your permission?

A. Yes. I really didn't know the details of how you go about registering it. All I knew is he was going to provide a service. And I couldn't have given him permission, when I didn't even know what he would do with it.

Q. When you say he was going to provide a service, what do you mean?

A. He was going to -- part of his business arrangements for his customers was to provide free either Web pages or Web domains for their use. And he would manage them in terms of putting the material up and paying for the rental and that sort of thing. Now, I expect him to use my name for registering the Website that I would be using.

Q. Which was?

A. Our-Agaricus.com.

MS. BOLTON: Mark this as Exhibit 3.

(Complaint Deposition Exhibit No. 3 was marked for identification).

BY MS. BOLTON:

Q. Mr. Isely, if you would take a look at this.

And this is Exhibit A to the complaint, to the Commission's complaint in this matter.

A. (Witness peruses document).

Q. Do you recognize what this is?

A. Well, it's an image of one of the pages off of Agaricus.net and it seems to be featuring questions or statements about RAAX11.

Q. And I just want to read from the first column here. Especially at breast cancer, the OPC Agaricus protocol shows that it works in 99.9 percent of all cases, even at late Stage IV it seems to work. From late 2004 to today, about 5,217 women took the protocol. Many doctors all over the world are reporting since he is using the OPC Agaricus protocol, nobody of his patient died. We received this positive message every day from all over the world. Now many, many patients entered into protocol from UK where many clinics started to use our special protocol. If you are living in the U.S., just call Mr. Isely and he will explain how it works or fill out form.

Now, were you aware that your name appeared on this page?

A. No. See, I explained earlier that I -- the reason for getting Our-Agaricus.com was to isolate myself from this aspect of his business. I was selling RAAX as

a dietary supplement. He was -- maybe legally in Brazil, I don't know, he was selling RAAX as a medicine. So I figured even the less I knew about what he was doing, the better. And the only reason I go to his Web pages after I got my own was to go to a shopping cart and check his prices, just to make sure mine were lower than his.

Q. And when you say, he was using it as a medicine, are you talking about for cancer treatment?

A. Well, he's talking about a cure here. And this may be a true statement. On the other hand, I'm not going to protect George Otto and prove it is. That's his business.

Q. Right. And when you say cure, you're talking about a cure for cancer?

A. Yeah.

MR. VAN HORN: You're talking about -- you're referring to the language she just read?

THE WITNESS: I'm saying the language right here is George Otto's and I don't pretend to protect him. That's his business.

Q. And in the second column, in the middle, it says, Even very resistant Leukemia cells die off, informations U.S.A., 828-369-7590. Is that your telephone number?

A. Yes.

Q. Okay. And, again, do you know how that got into this Website?

A. Well, obviously the person that had control of this Website with the password, the PIN number and the account number was the one, only one who could post that. So it wasn't me. And I have to assume it was George Otto, since he owns, runs the company. But I have no proof of it.

Q. Do you know if you received calls from consumers who got your number via this Website?

A. No, I don't.

Q. So, do you know if consumers ordered product from you because they got your telephone number via this Website?

A. I don't know that.

Q. And at the bottom, on the first page, where it says manufacturers FDA registered, is that referring to your registration?

A. No. George Otto, in order to import to the United States, had to register his facility as a importing manufacturer. And he told me he had done that, I believe, the --

MR. VAN HORN: We provided you with this.

THE WITNESS: You have that.

MR. VAN HORN: That's Otto's. That's our 00060.

A. "Manufactured FDA registered" is kind of an awkward phrase.

MR. VAN HORN: I want to meet this George Otto guy.

MS. BOLTON: I would like to mark this as Exhibit 4.

(Complaint Deposition Exhibit No. 4 was marked for identification).

BY MS. BOLTON:

Q. Okay. Mr. Isely, do you recognize Exhibit 4?

A. Well, I'm not familiar with the page. It appears to be another page off of the Agaricus.net domain.

MS. BOLTON: And I will add, this is Exhibit C to the Commission's complaint.

MR. VAN HORN: Thank you.

Q. And in the middle of the first column, where it says contact, there's an international telephone number, 828-369-7590, U.S. telephone number, 886-944-7359 and there's a fax number listed, 828-369-5861. Do those numbers belong to you?

A. Yes. They did at this point in time. I either had the tollfree number or the fax number.

Q. And at the bottom of the page, I'm just going to read it from the last paragraph. In a recent study, 91

women who were suffering from breast cancer at Stage IIIB or IV took part in our RAAX protocol. By April 2004, 41 women had totally recovered, 23 women were in remission, 27 were stable and only 9 had not survived. A survival rate of 91.27. If you would like to find out how you too can participate in our ongoing study in the U.S.A., call 828-369-7950. And, again, is that -- that's your telephone number; is that correct?

A. Yes.

Q. Okay. And what study does this refer to?

A. I have no idea. My personal belief is that George Otto was using this as a sales ploy because -- to try to get people to buy his product, but I've never seen a study. He never sent me anything like that.

Q. Did you get telephone calls from consumers that inquired about a study?

A. I think I had two and I told them that I didn't know what the study was and it was no part of anything I was doing.

MS. BOLTON: Let's go off the record for a second.

(Off-record discussion).

MS. BOLTON: I would like to mark this as Exhibit 5.

(Complaint Deposition Exhibit No. 5 was marked

for identification).

BY MS. BOLTON:

Q. Mr. Isely, do you recognize this document, Exhibit, is it 5? I'm sorry.

A. As a mailing envelope, flat rate, Priority Mail.

Q. And is that your return address on there, William Isely, Walnut Creek?

A. Yes.

Q. Okay. Do you recall sending out this envelope?

A. Not particularly.

Q. But is this -- do you typically, when you mail out RAAX product, is this typically how you mail it out, in an envelope such as this?

A. Well, when it's a small order like this, yeah.

Q. Okay.

A. This one obviously went through the sorting machine in the post office and got tromped on. First one I've heard about.

Q. But this -- do you acknowledge that you sent this out?

MR. VAN HORN: Is there any date on here or anything?

MS. BOLTON: Up at the --

MR. VAN HORN: Oh, there it is. January 10th.

A. It looks like I mailed it. It was marked

liquid.

MS. BOLTON: Next will be No. 6.

(Complaint Deposition Exhibit No. 6 was marked for identification).

BY MS. BOLTON:

Q. All right. Mr. Isely, to the best of your ability, given that this is very difficult to read, Exhibit No. 6, do you recognize what this is?

A. Recognize what?

Q. What this is, Exhibit No. 6?

A. It would appear to be an invoice for this bottle of RAAX that went to Fox Road.

Q. At the top, it says National Customer 3005. What does that number signify? Is this an invoice of yours that you would have sent out --

A. Yes.

Q. -- with a bottle of RAAX?

A. Yes.

Q. And what does that mean, National Customer 3005?

A. Well, I also had international customers, so -- but the actual number -- I'll try to remember. I started out -- and, of course, I have a lot of products that aren't RAAX. So that wouldn't -- that was 3005 order for RAAX. But I also had a break in the numbering system. I'm trying to remember how big the break was. Like I

might have been in the 1000 number at the end of a time period, I started over again with a 2000 serial number. And so there's not much to be gained or to be -- in terms of the number, other than it's unique. I wouldn't have two numbers that were the same. And then they increased with time, but there were gaps in there.

Q. Does this number refer to the number of the customer ordering RAAX, particularly?

A. No. The numbers increase sequentially by calendar time. In other words, if the next day after this one, if I had an order, it would likely have been 3006. I had some competition buying from me and sometimes I wanted to mislead them as to what I was doing, so I would put in a gap of maybe 50 between the time they bought and the next time.

Q. And on your invoices, do you typically include your e-mail address and your telephone number?

A. Yes.

Q. And at the bottom --

A. Uh-huh (affirmative).

Q. -- it says, William Isely, General Manager of Takesun, U.S.A.

A. Uh-huh (affirmative).

Q. Now, what does that mean?

A. I've explained in this here what Takesun U.S.A.

was. At one point it was the importing business name, Gemtronics was the retail. And although I generally dropped Takesun, U.S.A. after the time period when I had that partnership, I had a computer blank form that I would just fill out the details of this order and invoice, so I wouldn't type the whole thing all over again. And I had several blank forms and some of them have the Takesun, U.S.A. on there and some of them didn't.

Q. And on this, it's difficult to read, but it looks like method of payment, PayPal?

A. As I recall, this one was PayPal.

Q. Now, how would you know this was PayPal? How did you know this order was PayPal?

A. Because this order was sent to me in an e-mail from George Otto. And he would tell me in his e-mail that he had collected by PayPal. So I would know that the order had been paid for and I was authorized to send it out. He wasn't necessarily going to pay me, but he wanted to know that it was, it was clear it could be sent out. It wasn't being held up for lack of payment.

Q. Now, when you say it wasn't clear that he was going to pay you, what do you mean by that?

A. On these sample orders, this is obviously a sample order, somebody buying one of a kind. The reason

that I was asked to do it was that selling a sample order of one from Brazil -- if it had been a lucrative order, like 10 bottles or something, I never would have heard of it. He would have supplied them from Brazil. But for one bottle, it would cost him more to send it than he was getting because of various fees, like exporting, customs, banker's fees on collecting the money and whatever. So he would ask me to send that sample or fill that sample order as a drop ship. And this was a drop ship.

Q. And sample order, you just meant, again, like if it was one bottle?

A. Yeah.

Q. You call that a sample order?

A. Yeah, yeah.

Q. So he would ask you to send it out?

A. Send it from my stock. And he -- even though it would cost me $7.00 to send it, and so I would do that. And sometimes he reimbursed me and sometimes he didn't. And in this case, my records don't show that he reimbursed me.

Q. And why would you fill an order that you wouldn't be paid for?

A. Well, I had a profitable business and it was based on being able to buy from this guy. And I wasn't going to quibble over one or two bottles a year, if he

didn't pay for them.

Q. And how would it benefit you to fill this order?

A. Well, probably the most benefit was maintaining a good relationship with the company that was supplying me with $5,000 or so of stock a month that I was paying for, of course, which was -- I was able to make a business. It's like people give samples away. It's a matter of building good relations or maintaining good relations.

Q. Did you think that there was the potential that if this person were to order the product again, they would order it from you?

A. Well, they might. You know, they are free to go on the Web and find out what their prices are. I think if they did that, they would probably buy from me because that was my, that was my business model, have the low price.

MS. BOLTON: Let's go off the record for another second, if you don't mind.

(Off-record discussion).

(Complaint Deposition Exhibit No. 7 was marked for identification).

BY MS. BOLTON:

Q. All right. Mr. Isely, this page is Exhibit 7.

A. Yeah. This one?

Q. And do you recognize what that is?

A. Yeah. This is an Express Mail, otherwise it's the same as the other one. That's one I sent to -- it's for one bottle of RAAX. Method of my getting the order was the same as the other one. I got an e-mail message that said please drop ship this and also informed me that it had been paid for by PayPal.

Q. And that e-mail message would have been from Mr. Otto?

A. Uh-huh (affirmative).

Q. Okay.

A. I know the customer likes to have a receipt for what he bought, so even though I didn't receive the money, I knew about how much they paid for it, so I would include that on the invoice.

MS. BOLTON: Okay. And I would like to mark this as Exhibit 8.

(Complaint Deposition Exhibit No. 8 was marked for identification).

BY MS. BOLTON:

Q. And would this be the invoice that you were referring to?

A. Yeah.

Q. Now, do you know if you were compensated at all or do you know that you weren't compensated from Mr. Otto

for this order?

A. Well, George Otto was very irregular about -- and it wasn't very often that he had anything to pay me for, but in that time period I don't have a record of receiving PayPal payment from him. I have -- he owed me some shipping. He paid me, I think, some months after this, he paid me for shipping some products he had sent me by mistake. I was holding them, asking him what was I supposed to do with them. Eventually he had me send them to Europe. I think that's the -- in my PayPal account records, that's where I have it, but I can't identify these.

Q. How frequently would Mr. Otto ask you to either fill one of these, what you call a sample order --

A. Uh-huh (affirmative).

Q. -- or a larger order?

A. Rather infrequently. I would -- I think I went back in that two-year sample period that I mentioned, and I think in the second year back there weren't any. And these two were probably -- I mean, very frequently, you know, it might be six, eight months apart before I got to having these two so close together. I thought at the time, hey, I wonder what's happening.

Q. And let's go back to the invoice. You have a note at the bottom of the invoice.

A. Uh-huh (affirmative).

Q. Please order direct by phone or e-mail in the future.

A. Uh-huh (affirmative).

Q. And why did you put that in there?

A. Well, it was kind of cumbersome to get orders from George. And I preferred to get them directly. And normally, in this case it wasn't -- George was running a special, but normally I'd be able to offer customers a special price.

MS. BOLTON: Mark that as Exhibit 9.

(Complaint Deposition Exhibit No. 9 was marked for identification).

BY MS. BOLTON:

Q. Mr. Isely, I'm showing you Exhibit 9. Do you recognize what this is?

A. Yes. This was front side of my brochure.

Q. And is this the brochure that you were referring to earlier that you put together?

A. Yes. My brochure was dynamic, as I told you. As products changed, different products would be on here. And --

Q. But this is something that you created?

A. Uh-huh (affirmative).

Q. Is that correct?

A. Yes.

Q. I wanted to draw your attention to the lower left-hand portion, where it says, For more information, go to Website, go to www. Agaricus.net, click on U.S. sales. So why did you direct customers to go there for, to purchase?

A. This was really archeology, in a way. This is what I had put on there when I had my earth -- Nature First link and I just hadn't taken it off. This didn't go -- in this time period, this would go nowhere because there's no U.S. sales on the home page. They have a U.S., which -- but it doesn't go to my pages. And so just a matter of omission, I hadn't removed it. But people would be mystified looking for U.S. sales button on Agaricus.net. If you look at the home page, you won't find it. The U.S. they put on there in place of it was to go to English speaking pages that George was using to sell directly to American customers in competition with me, so --

Q. But at one time, if you went to Agaricus.net and you clicked on U.S. sales, would that go to you or to your Web pages?

A. It would go to the Nature First Web pages that we talked about that were in existence for about two years and were taken down six years ago. There's another

artifact on here, which is the Takesun, U.S.A. And Takesun do Brasil is part of a sentence. I just highlighted it so -- because people expect to know who makes the products they are getting. So I left the name Takesun on there. It says Takesun do Brasil, then packages the mushrooms in various ways, so on, so on.

Q. And in the middle column --

A. Uh-huh (affirmative).

Q. -- the third paragraph down --

A. Yes.

Q. -- it says, Agaricus blazei Murill mushrooms were found to have other beneficial properties as well. Besides immune enhancing, they are anti-tumor, interferon and interleukin enhancing, anti-viral, cholesterol reducing, and a blood sugar modulator. You said you wrote this. What do you mean in that paragraph?

A. I was just listing phrases that I found in the, some of the reference documents on Sloan-Kettering, on the Agaricus, on their Web pages where they have about 13 articles listed of characteristics of the Agaricus blazei Murill mushroom.

MS. BOLTON: I need to mark that as Exhibit 10.

THE WITNESS: That's my best recall. That was what -- that language probably goes back to when I first created this about eight years ago. So I'm a little bit

fuzzy about which article or -- but I'm pretty sure it was Sloan-Kettering.

(Complaint Deposition Exhibit No. 10 was marked for identification).

BY MS. BOLTON:

Q. Mr. Isely, I'd like you to look at Exhibit 10.

A. Uh-huh (affirmative).

Q. And do you recognize this document?

A. Yes. This was a thing I created at a time, let's see, a little more than a year ago. George was pushing e-mail I'd get from him, what he called the RAAX/Agaricus OPC Protocol, which was a schedule of use of certain dietary supplements that were common in some institutions in Europe. And he was talking about curing and remission and using terms like that, and as a result of what he called a study.

It bothered me because they didn't go so far as to have double-blind control. And the reports -- I tried to find out from him, is it really true? You know, what medical journal's reporting it? And I never got any answers. And so in my mind, the data was no better than just group testimonials.

But somebody who was buying RAAX -- my preferred method of dealing with a customer was to talk to them and explain that I was just selling dietary supplements and

that I didn't -- wasn't giving them medical advice. And if they wanted to buy it, they should recognize that I was not representing it that way.

And occasionally people would go to Agaricus.net and eventually order product. And like these box shipments, I didn't have an opportunity to talk to those people. And so my approach on that, substitute for a conversation, was to reduce what George had been putting out as a sophisticated study as to be no more than testimonials.

So I changed the terms of the things like, improvement or no improvement. I mean, what does that mean? It means you don't have a headache today or, you know, your nose is no longer dripping or whatever. And give them a more objective view of what is here, at least in terms of the degree of sophistication with which the results were reported.

Q. So did you create Exhibit No. 10?

A. Pardon me?

Q. Did you create this?

A. This was actually something that George sent me. And I wouldn't use it the way it came. It's the same as he sent me, except his description of the improvements, in his case it was remission or cure or, you know, no change. And that that is getting into what I consider to

be medical descriptions. I wanted to correct that impression that people might have had that led them to buy this product. And when I was drop shipping, I was adding this as a necessity to that.

Q. So this is your version of the --

A. Yeah.

Q. -- data that George supplied you?

A. Yeah. I tried to make it -- well, I think he had it on his Website, too. I was -- my idea was to concert it to a testimonial level. And I think, I think I did that.

Q. Okay. So you are confirming that you did, in fact, create this; is that correct? I mean, you printed this up, you --

A. I printed it. But the data is, data is -- other than the labeling of the columns, it's data that George gave me.

Q. And this is something that you submitted in packages of product that you shipped to consumers?

A. Only, only when they had already bought the product and I didn't have an opportunity to explain it to them, which was the case of the two box shipments. That was a very unusual circumstance I run into where I used it. I did not use it for advertising or try to get sales from it, but I figured if these people were buying anyway

and wanted to continue to buy, then I'd offer them the low price. That's why the price was on there.

Q. In the second sentence here, it says, The RAAX11 Agaricus OPC Protocol for Stage IV conditions is the taking of 500 ML of RAAX11 and 1000 ML Agaricus OPC over a period of a month. What do you mean by Stage IV conditions?

A. I lifted that from George's material. I guess I'd leave it up to people to decide what they -- in other words, it's a testimonial, it's ambiguous, and I want people to recognize that.

Q. But what does Stage IV conditions refer to?

A. Well, typically people use that for talking about cancer. And I'm sure George was.

Q. And in the last sentence in that paragraph, it says, for cases at lower levels, such as Stage II, et cetera. What does Stage II refer to?

A. Well, that would probably refer to cancer as well.

Q. And in the next paragraph, the second sentence -- well, let's start with the first sentence. In the past it has been hard to collect --

A. I don't know where you are.

Q. I'm sorry. The second paragraph.

A. Okay.

Q. In the past, it has been hard to collect meaningful results other than occasional testimonials. It was difficult to tell if the users followed the protocols, and in most cases were not observed by health professionals. One study using the older RF1000/RAAX11 Protocol yielded a successful response in 80 percent of breast cancer cases over a one-year period. What study does that refer to?

A. That's the one that you brought up somewhere earlier in one of the Web pages of George's, where he talked about, I think, 91 women. I think that was a European study in Dr. Schnookles' laboratory somewhere or clinic in Germany. I think, I think that's identified on some of the material that you imaged, that you sent me.

Q. Okay. And the second to the last sentence?

A. You notice I point out that it's difficult to tell because the cases were not observed by health professionals.

Q. The second to the last sentence in the paragraph before the graph, the information on RAAX11/Agaricus OPC Protocol covers over 1000 cases and is tabulated below. Did you do that tabulation below?

A. That was -- other than the labeling of the columns, that was material that was, by George's account, was collected from three clinics in Europe. I think one

in, let's see, one is, I think, in Spain, one in Switzerland and one in Germany.

Q. And then it says, for more information, contact William H. Isely, then it has your e-mail address and your -- that's your telephone number?

A. Yes.

Q. Okay.

A. And I put that in there particularly to be able to make sure that they understood the nonrigorous nature of this study. That they probably encountered a different version of it before they bought the RAAX on George's Website.

Q. And there's a graph below, and it says -- it starts, condition, number of cases, number responding. All of these conditions, what kind of conditions are they referring to?

A. Well, I guess, the conditions in the -- well, George has listed just about all the organs of the body that -- conditions that are nonoptimum. I didn't know.

Q. Are these referring to cancer, as far as you know?

A. I don't know. I would presume so.

Q. Okay. And in the upper right-hand corner where it has the price for RAAX, was that your price for RAAX, $119 per bottle?

A. At the time this was published. I sold it as cheaply as about $50, when I was closing down the company, but this is before that.

MS. BOLTON: Okay. We'll mark this as Exhibit 11.

(Complaint Deposition Exhibit No. 11 was marked for identification).

BY MR. BOLTON:

Q. Mr. Isely, I'd like you to look at Exhibit 11. And can you identify what this is?

A. What are you looking at?

Q. That piece of paper.

A. Well, this is the back side of the --

MR. VAN HORN: Back side of Exhibit 10?

THE WITNESS: Not that. It's the back side of the brochure, right.

Q. Exhibit 9. Back side of Exhibit 9?

A. Yeah.

MR. VAN HORN: Okay.

Q. So as the back side of Exhibit 9, this is part of a brochure that you put together and printed out?

A. We're talking about the same thing? You're talking about this?

Q. Yes, talking about Exhibit 9.

A. You're looking at something else.

Q. No, no, mine is just in black and white. I wanted to give you the color version.

A. Yeah, this looks like the back of mine.

Q. Okay. And, again, this is something that you sent to customers in their orders, in their shipments?

A. Uh-huh (affirmative).

Q. In the middle column it says, Extract for Therapy Purposes. What therapy are you referring to?

A. Whatever the person wants to use it for. I had customers who were therapy specialists and so I would assume they were buying for that reason, but I didn't know what their therapies were.

Q. All right. As far as you know, is RAAX11 used for any particular therapeutic effect?

A. Well, you have to ask the people that buy it. I'm not, I'm not a therapy person and I don't treat people.

Q. And it says in the last paragraph, in the middle column, Depending on their status, people who take the extract for therapy reasons may use up to 10 bottles of it in a month. For preventive purposes many people normally will use one bottle a month.

For prevention of what? What preventive purposes are you referring to?

A. Well, this ratio of 10 to 1 is really based on

my experience with customers. I'm just passing that on. Some people will want, will want to use 10 bottles a month, and some will just take a half a teaspoon or a teaspoon a day and use it for one month.

Q. And what would they be looking to prevent?

A. I don't know. You know, I was in the business of selling dietary supplements that people wanted to buy and that was basically all I needed to know to run my business. Now, some people would volunteer things. And over the long period of time, I would learn what a lot of people thought, which is quite variable. And some people talked about prevention. They said they wanted to buy it for prevention. Fine. You're the one who is deciding why you want to buy it.

(Complaint Deposition Exhibit No. 12 was marked for identification).

BY MS. BOLTON:

Q. All right. Mr. Isely, you have in front of you Exhibit 12.

A. Yes.

Q. All right. Do you know what that is? Can you identify that?

A. Well, it's another WHOIS read out, and this one happens to be on domain Our-Agaricus.us, which is our, you might say, the mirror Website to Our-Agaricus.com.

Q. Are you --

A. The idea was that whatever is on Our-Agaricus.com will automatically be put on Our-Agaricus.us, just so somebody searching on the Web will have twice the chances of finding you than if you just had one.

Q. And is this a Website that you agreed with Mr. Otto that would be your domain, that you would use to sell your product?

A. Your domain is ambiguous because he maintained control of it. It was for my use, but I wouldn't say that it was my domain, in terms of owning it, because he had the credentials that were required to post anything on it.

Q. It lists your name as the registrant?

A. Uh-huh (affirmative).

Q. Is that correct? And is that your address and toll phone number listed as well?

A. And it lists my e-mail as georgeotto@takesun.com.

Q. And is this -- I'm sorry. Go ahead.

A. Which says that someone else, George Otto, actually did the registration, even though he put me down as the registrant.

Q. Is this a domain that you agreed to have your

name put on?

A. Let's see. I didn't agree in terms of an actual incident in which I said, yes, do it. I guess by asking for him to get me a domain that indirectly I agreed for him to do it.

Q. Did you ever independently get a domain name on your own?

A. Yes.

Q. And what was the name of that?

A. About six weeks ago, in terms of educating myself about domains, I bought one for $9.99. And it was called convertacar.com. And so I went through the whole process. There were 10 steps to actually get the domain. And the only important step was when I paid for it. Because when I paid for it, I then had a password, I had a PIN number and I had an account number. And after I got done, I went back and I found that by using those tools, I could, again, get access to my domain.

I did not put it on a server. Actually, a domain is worthless unless you find a server and have it installed. And that's another step which also has its own security steps.

Q. And from what period of time did you post your information on Our-Agaricus.us?

A. I didn't post it. I explained to you that

George Otto posted it.

Q. But did he post information that you asked him to post?

A. Yes.

Q. Okay. And this is information that you supplied to him?

A. In a general way. I didn't, I didn't lay out formats. You know, I didn't -- I would say, I want a picture of this and a picture of that. And some people will actually design their own Websites in Web language which I'm not familiar with and then all you do is like attach it to an e-mail, you just put it onto a Website. But I don't know how to do that. I didn't do that.

Q. And was this a Website from which consumers could place orders for product from you, from RAAX11, for instance, from you, for you?

A. It was a mirror image. It did exactly the same things that .com did.

Q. That Agaricus.com did?

A. Our-Agaricus.com.

Q. Our-Agaricus.com. Thank you. And by that, you do mean that consumers could order products from you from that Website?

A. Yeah. I never really thought about the second one, because I think, in fact, when you went to -- I

never did this. But I believe the way it works is when you go to our-Agaricus.us, it just links to Our-Agaricus.com. In other words, it's sort of a ghost Website and collects people and then funnels them over to the other one. So, in effect, there was probably only one Website that was active, that was actually involved in a -- that related to customers. I found out yesterday that George has 15 Websites. And I think most of them are of that nature. I don't think they are stand-alone, they just -- you have 15 times as many chances that somebody is going to find you, when they are -- you know, if we're on, if you were trying to get people to hit on Agaricus, for example, there's 998,000 Websites that will tell you something about Agaricus, if you go searching for that. So your chances of being found are very small.

Well, you can increase your chances by just having more Websites. But they are not necessarily going to add anything to the other Websites. Of course, the real way to get there is to pay the -- you pay to have your Website put near the front, so that people will see it right away, won't have to click down 2000 pages to find you.

MS. BOLTON: Okay. Mark that as number 13.

(Complaint Deposition Exhibit No. 13 was marked for identification).

BY MS. BOLTON:

Q. And, Mr. Isely, I'd like you to look over Exhibit 13, and can you identify this?

A. Well, this is something put out by a company called Internet Corporation Listing Service. And they get paid for e-mail rentals. See, when you so-called buy a domain, you're only renting it. It's like .com is one set of domains. And somebody somewhere has all, has a listing of like a phone book of every domain that says .com, to make sure that nobody duplicates domains. And you're offered two years, four years, ten years of rental when you sign up for a domain. But eventually that rental comes due. And the people that rent domains are actually brokers. They are not the people -- they are not the .com.

The .com is just one place, but there are many people. Like many real estate people can sell a house. Many of these Internet brokers can register or re-register when the rental has run out. And so this to me looks like a form that somebody was sending out to probably thousands of domain registrants. And the way they know when to send them is do a WHOIS. It will show you when that thing is going to run out, so just ahead of time they send you -- and they hope that their price of renting you will be cheaper than the one you're paying so

that you'll switch over. And this was sent to me because of some domain. I have to find out which one.

Q. The domain at the time, it says RAAX/Agaricus.com?

A. Oh, okay.

Q. And is that -- was that a domain that was registered in your name?

A. Probably was. I wasn't aware of it. But I said -- I checked yesterday and something I clicked on showed me that George has 15. So I know he had registered three of his domains in my name. And I wasn't, I wasn't aware of this one.

Q. So is this -- this is not a domain that you registered or it is a domain that you registered?

A. I didn't register. This is registered by George. Let's see if it says somewhere. No, this guy is -- this is not a WHOIS, this is just somebody that's trying to take George's Website away from whoever has registered at the time before.

Q. Well, it's mailed to you.

A. That's because George put my name down.

Q. Okay. So it looks like a bill.

A. I think somewhere it says, This is not a bill. It says, This is a solicitation --

Q. Okay.

A. -- for the order of goods or services and not a bill, invoice or statement of account. You're under no obligation to make any payments. When you get one of these, you know it's a guy trying to take the business away from the guy that has it.

Q. But is it your understanding that this was sent to you because you were the -- listed as the registrant of the domain?

A. That's my assumption.

Q. But it's your testimony that you did not register this domain?

A. No.

MS. BOLTON: Mark this as Exhibit 14.

(Complaint Deposition Exhibit No. 14 was marked for identification).

BY MR. BOLTON:

Q. Mr. Isely, I'd like you to look at the document that's marked Exhibit 14. It is a WHOIS search result for the domain Takesun.com.

A. Takesun is the mother company of Agaricus. I think it's where they keep their -- if they are a corporation or whatever, where they keep their business.

Q. Now, if you look on the second page, where it says the registrant --

A. George Otto.

Q. -- at 964 Walnut Creek Road, Franklin --

MR. VAN HORN: Does he live at your house?

Q. -- 28734.

MR. VAN HORN: Has that been redacted somewhere in there?

MS. BOLTON: No, that's exactly how it came out.

MR. VAN HORN: You see that?

MS. BOLTON: No. I know, it looks like that.

MR. VAN HORN: It's just something. I got you.

MS. BOLTON: But not by us. That's how it printed out.

MR. VAN HORN: That's just strange.

BY MS. BOLTON:

Q. And that's your home address; is that correct?

A. Yes.

Q. Okay. Did you give Mr. Otto permission to use your home address --

A. No.

Q. -- in the registration of this domain?

A. No, I didn't.

Q. Okay. And you are listed as the administrative contact --

A. That's interesting.

Q. -- at your home address. And, again --

A. My name misspelled again. I think you'll find

almost every one, where he misregistered it without my permission, he probably did them all at the same time and misspelled my name. Every time it's misspelled like that.

Q. And the e-mail address next to your name on the administrative contact, Webmaster at Agaricus.net; is that your e-mail?

A. No, that's Brazil's Website. The Webmaster for Agaricus.net, the guy that changes the prices of things on Agaricus.net would be George Otto.

Q. And have you ever seen the Website Takesun.com?

A. Yeah, about eight or nine years ago. I think that was the first Website that I found for George. And he -- Takesun's main business is bulk wholesale. At that time he was a bulk wholesaler of commodities. You know, so many kilo, so many hundred kilos of peppers or ground nutmeg and stuff like that. And last night I was just Googling around and I found his Takesun.com now has Agaricus mushrooms on it, probably the rest of the Agaricus products, but I didn't spend much time looking.

Q. Did -- when you sold RAAX products, did you sell them wholesale or just retail or both?

A. That has a gray answer. I didn't have a straight schedule that says these are the retail prices or these are the wholesale prices. I did have a price

list that was -- I used actively up until about two years ago, which gave a price in terms of a discount based on the dollar value of the order. If the order was more than 300, I think they got something like 15 percent off the retail price. And if it was over 600, maybe it was 25 percent.

After a while, I felt the prices were just too high at retail and I basically was selling at one price which everybody -- in terms of profit, it would have been the wholesale price. In other words, $120 for a bottle of RAAX was the same price that someone would pay if they bought 10 bottles or bought one bottle.

Q. And did you fill large orders for the product?

A. Occasionally.

Q. What would you categorize as a large order?

A. Of RAAX? A dozen bottles. That would usually go to somebody who was reselling them themselves. Individuals wouldn't buy that many at once.

Q. And would these typically be stores that would be purchasing them from you or --

A. The names sounded to me like they were more than a home business. In other words, it would be -- it might be a center or something like that. Might be a health food store, but you can't always tell from the name.

Q. And the only way you would know would be because

of the name?

A. In a couple cases we've had reason to discuss what kind of business they were in, so I would know that way.

Q. Did you ever have distributors as part of your business?

A. I tried to set up distributors back in -- formal distributors. I had a distributor agreement form when I first started with -- I had an agreement with Jane X, for instance, which was back in 2000. The main thing I was interested in was that they didn't represent the products for medical purposes and that they paid their taxes. Those are the two main reasons that I wanted them to sign. But it seemed to pull out of vogue if people would sign up as distributors. The ones that bought in quantity already had their own businesses, I think, and didn't want to think of themselves as a distributor of somebody else. So I'm not sure that -- I don't think anybody signed a distributor form for me in more recently than maybe six years. I sent them out a couple of times.

Q. And when you sent these out, were they under the name Gemtronics or did you send them out as individually?

A. Well, back originally they were under Takesun U.S.A., when I was, when I was trying to build a business, which was just wholesale. And that's when I

worked up the distributor form. And I think that some people would sign up. I frankly can't tell you whether I changed it or not, because the name is Gemtronics now. I don't remember.

MS. BOLTON: And this will be Exhibit 15.

(Complaint Deposition Exhibit No. 15 was marked for identification).

BY MS. BOLTON:

Q. All right. Mr. Isely --

MR. VAN HORN: Exhibit 15.

Q. -- you have Exhibit 15, which is a WHOIS search results for domain OPC-Agaricus.net. Are you familiar with this domain?

A. Never seen it before. It's a very interesting document, though. I notice something different from the others. It tells me something about the intent of George Otto, which I've never been able to figure out, other than I know he's lying. This one was created in June of 2006. He told me that in 2004 he made a mistake and that's how my name got attached to these domains. But here two years later it's done again, so I think it's intentional.

Q. All right. And you're referring to the fact that your name and address and telephone number appear as -- under the registrant category, the administrative

contact and technical contact listings?

A. Yeah, right. But, again, he is using his e-mail address after my name.

Q. So you are -- is it your testimony that you're not familiar with this domain or any Website that it may pertain to?

A. That's correct. I wasn't even aware it existed. But it's one of those so-called 15 that I stumbled on yesterday. I stumbled on a listing that said Takesun and had 15 domains. It didn't list what they were, but this is another one, I guess.

Q. And let's talk about Mr. Otto for a second. And I'm referring to George Otto Kather. And you -- we seem to mutually refer to him as George Otto. And I don't mean to repeat myself, but how did you get to know him?

A. I was looking for a reliable source of Agaricus blazei Murill, which I had difficulty buying in the United States because the only people that had it were health practitioners that basically bought it for their own clients, and sometimes didn't have enough stock to share with anyone else. And so I just got on the net and was surfing around until I ran across what looked like somebody who was anxious to sell to English-speaking people.

And I confirmed with one of the health

practitioners that that was the source that they were getting it from. So rather than wait for six weeks before I could get my product for myself and maybe not get it at all, I decided I could import it, also.

Q. And this was approximately when?

A. 2000.

Q. And you said you were a -- you were an importer for Mr. Otto or importer of Takesun products; is that correct?

A. I became an importer with Takesun product.

Q. And as far as you know, you're not the sole importer --

A. No.

Q. -- in the United States?

A. Oh, no. George Otto is quite aggressive in having other distributors. In fact, he did get some that were stupid enough to sign his agreement and showed up on Web pages as representing distributors of Takesun in the United States.

Q. And what was the extent of your business relationship with Mr. Otto?

A. I described that before as basically a buyer of products from a foreign manufacturer.

Q. For the purposes of resale?

A. For the purposes of resale.

Q. Did Mr. Otto help you in any way with your business, other than before when you mentioned the two domains that you, that he registered with your permission?

A. No. He tried to -- he offered, offered me his brochure, some of his advertising material, which I rejected out of hand. First place, because they were not written in good English, but largely because they were -- they reflected the medical claims that he had on his Website, which I knew were not proper for the United States.

Q. Did he provide you with any technical assistance, in terms of setting up computers or access to the Internet or anything of that nature?

A. It wouldn't have been feasible, let alone I didn't want to. To do that from Brazil with his lack of English skills, it was hard enough to order from him. I mean, we went through sometimes three or four e-mail responses back and forth before I could get a simple number of what I wanted in the order and when I wanted it. I mean it, was bad enough to order from him, I didn't want to complicate that with anything else. And looking at his end product, his Web pages aren't really the best. So there would be no reason from that point.

Q. Did he at all facilitate your setting up the FDA

registered warehouse for the product in the United States?

A. Again, this is a gray area. I can't say -- I'll explain it, rather than say yes or no. He was required as an importer of the United States to engage what's known as an FDA special agent. I hope you know what they are.

Q. (Shakes head negatively).

A. This came about, I think, because of Homeland Security requirements that anybody importing to the United States -- well, let's see. Exporting. Got to get the words right. Anyone sending products to the United States that were either food or for dietary supplements, was required to engage what you might call a broker. They were usually and quite often ex-FDA employees who were familiar with FDA regulations and products and categories of codes of foods and so on. And these agents had to maintain a 24-hour office.

Let's say some product came in and there was some question about maybe a safety issue of what was in this product. They wanted somebody they could call on a 24-hour time period that would be able to -- that would know more about George Otto than was on file. And could act for him. If it was necessary to dispose of, for security reasons, to dispose of the item that they had

prior permission to act for him. This was with the understanding that sometimes hard to get in touch with somebody in a foreign country and you don't know who they are and these people were bonded agents for doing that purpose. And you had to pay a fee for that.

And in the process of his doing that, he mentioned to me that this broker company, whatever you want to call them, special FDA agent, would facilitate my registering my business as an FDA food warehouse. I found out since that I could have done that myself, if I had known. I mean, all you needed to do was know where the Website was to go to do that. But this agent that he had engaged for another purpose helped me do that. So it was indirect help.

Q. Do you still maintain an FDA registered warehouse?

A. Let's say that I haven't canceled my registration with the FDA. I don't think -- I don't maintain my house for that purpose any more, but I could start importing again and I guess I would still be on their list of approved warehouses, because I haven't told them I'm not doing it.

Q. Now, you mentioned in your -- there was a reference in your Answer to Interrogatories about redesigning labels for Takesun products; is that correct?

A. (Nods head).

Q. You have to give an audible response. You can't nod your head. She can't take that down.

A. Yeah.

Q. Can you explain what that was all about?

A. I was turning my head, because one of my ear phones was buzzing.

Q. Oh, I'm sorry. I thought you were nodding.

A. Let's see. The question was --

MR. VAN HORN: She'll repeat it.

Q. Oh, yeah. Explain to me about the redesigning labels.

A. Oh, yeah. Oh, yeah. My first large order as Takesun U.S.A., which was a joint order between myself and with Jane X. I'm trying to remember. It was 3- or $4,000. And up to that point in the small quantities I'd bought it come through okay. This was a big order. You know, probably weighed 40 kilos or something.

Q. And this is of Takesun products?

A. Takesun products, which I had gotten before, but this is my first big order. Came in to Miami and I guess they picked it to inspect. And the FDA would not pass it because there's a special form that goes on --

MR. VAN HORN: It's that FDA product code there.

A. Not only that, but you've got to say what a

serving size is and how many servings are in a bottle and what it contains. And whereas George's labels were -- what he'd done is taken his previous labels and I think he'd done a literal translation. I didn't know who he had translate it for them. But anyway, there was some violation of the method.

FDA is very specific. You leave out a comma and it's bad. Or if you don't identify the preservative, just say preservative, they knock you on that. So anyway they said, we're rejecting this, this order, this shipment, have to go back. So I talked to Takesun. And Takesun said Brazilian company doesn't allow products to be sent back. So here I had spent about $5,000 and products were stuck in Miami and I couldn't get them back to Brazil.

And so there were several back and forth discussions with the FDA, as to how we could salvage the shipment. And they said, well, if you get proper labels that pass our requirement sent to Miami and have your agent go in there under -- in other words, my broker, go in under supervision of the FDA, they allow you to remove the old labels and put on the new ones. And so between myself and Takesun, we got the labels corrected. He printed them out, sent them to me. I sent them down to Miami to the -- I think it was DHL was the shipper, I

believe, at the time. These were still in a bonded warehouse. I mean, and they are in the bonded warehouse. He spent a couple days with -- cutting open boxes. I think there were five boxes involved. And re-labeling every bottle, every bag, every whatever. And then he passed them and I finally, after about six weeks delay, I got my shipment.

Q. And did Takesun continue to use the labels that you designed, thereafter?

A. Oh, yes. Matter of fact -- well, let's see. Almost eight years went by without any question of the labels. Now, there were sometimes they would pull off a product and they would send it to a lab and it would get delayed a couple weeks. It always passed. But sometimes a new agent for the FDA would come in who wouldn't recognize the Pinnacle names that were on the label and I would have to -- they would get in touch with me, I would have to send literature to describe what the thing was so that they could accept it.

On the very last order I had, which was not -- it was not for RAAX, it was something else. They noticed something that had slipped by them for eight years, and that was that in the area where you say, preservative, that's all it said. Now, normally you say, preservative with what the name of the preservative was. And that had

been left off. And they said, well, the next time you buy this, make sure the label had been changed. And they put it through with the label.

Q. And when is it you did this label redesigning, approximately?

A. Well, since it was my first large order, that would have been in the year 2000. I'm not telling you that from looking at the documentation of the letters with the FDA, but I'm pretty sure that's when it was.

MS. BOLTON: I'm done. I'd like just a couple minutes to look through my notes and I might have a couple questions, but that's pretty much it for me.

MR. VAN HORN: All right.

(Recess taken from 1:50 p.m. to 1:53 p.m.)

MS. BOLTON: All right. We're back on. I've concluded my deposition. Thank you, very much, Mr. Isely. I appreciate your attendance and your answers.

MR. VAN HORN: All right. I'm just going to ask him a couple questions, go over a couple documents here.

(Respondent's Deposition Exhibit No. 1 was marked for identification).

EXAMINATION

BY MR. VAN HORN:

Q. All right. This is a four-page document or

four-page exhibit. It's actually two documents. And I represent that I've pulled this from the North Carolina Secretary of State's Website. I think you've probably seen these.

I don't have a copy for you.

MS. BOLTON: That's all right.

Q. I just wanted to get this into the record. You just want to take a second to look at that? I'll represent to you that that's information pulled from the North Carolina Secretary of State Website regarding the corporation Gemtronics, Inc. And you're holding the last two pages.

A. This is what I filled out.

Q. Okay. That's what I was going to ask you. You're holding the last two pages of this exhibit. This exhibit contains four pages. And these are Bates Nos. 0054 and 0055, respectively. Are you familiar with this document?

A. Yes.

Q. What's the title up there?

A. Articles of Incorporation, State of North Carolina, Department of Secretary of State.

Q. Okay. So you want to flip to the second page here, or the fourth of the exhibit. That's your signature down there?

A. Yes.

Q. And --

A. That's my signature.

Q. And there's a stamp under it that says incorporator?

A. Yes.

Q. So you formed or you caused the corporation, Gemtronics, Inc., to be formed; is that correct?

A. That's correct.

Q. Okay. And that was -- the document speaks for itself, but September 20th of 2006; does that sound about right?

A. Yeah. That was right after our visit to Raleigh in the summer to discuss this with my oldest son.

Q. Okay. Have you ever done anything else mechanically or administratively with regards to this corporation since you caused it to be formed?

A. I investigated what it would take to keep the accounts and turn in the tax forms for a corporation.

Q. Okay.

A. And I had thought that I had somebody who had the software to do it for a very low cost, but that source disappeared. And the cost of then continuing with the corporation looked exorbitant to me and I wasn't about to learn how to file taxes for a corporation, so I

thought of an alternative which would be a Limited Liability Company.

Q. Uh-huh (affirmative).

A. And neither one looked attractive, and so that was the end of it. I never went further with it.

Q. Okay. Now, this page three of the exhibit, line two, I'll represent states that the number of shares of the corporation was authorized to issue was 10,000; okay? You understand what that means, the number of shares the corporation --

A. Yes.

Q. So it's authorized to issue 10,000, according to the stock. Have any shares ever been issued?

A. No. They insisted I had to put some number down. That was just an arbitrary number. But no shares existed.

Q. Any members of -- any board of directors?

A. No officers, whatever, other than myself as the agent that sent the application to the state.

Q. Did you ever obtain a Federal tax ID number?

A. I did not.

Q. Did you ever obtain a state tax ID number through the Department of Revenue, State of North Carolina?

A. No.

Q. Have you ever executed any documents on behalf of this company?

A. No.

Q. For instance, a contract --

A. No.

Q. And --

A. No bank account, nothing.

Q. All right. So for all practical purposes, it's an inactive corporate shell; is that correct?

A. Oh, yes.

Q. Have you been filing your annual reports, to your knowledge?

A. I'm supposed to file an annual report on a corporation that hasn't come into existence?

Q. Well, these are legal terms.

A. Oh.

Q. In effect, it has come into existence, because you formed it.

A. Oh.

Q. And --

A. But there's nobody to fill out a report. There's no board of directors. Who is going to do it?

Q. Yeah, that's an interesting question. Well, I'll just represent that the state law requires that at the end of each year, you have to file what's called an

annual report, and you have to pay a $25 fee.

A. Who is required to? Which officers of the corporation is required to do it?

Q. Somebody has to. But the answer to the question is, that has not been done; is that correct?

A. That hasn't been done.

Q. All right. Here's that.

A. Now I just committed a misdemeanor or something.

Q. No, you didn't. They just dissolve your corporation, is what they do.

MS. BOLTON: Do you want me to wait till your done for any follow-ups I have?

MR. VAN HORN: Oh, if we're on that subject now, if you want to go on, just to keep it consistent.

EXAMINATION

BY MS. BOLTON:

Q. If you registered -- Mr. Isely, did you register Gemtronics as a for-profit corporation?

A. Yes.

MR. VAN HORN: Hold on. I'm going to object to that question just because -- I don't think that -- well, just the term --

THE WITNESS: I'm not sure.

MS. BOLTON: We can do it in the negative. Did you register it as a not-for-profit organization?

MR. VAN HORN: I'm not objecting -- the only reason I'm objecting is the terminology assumes facts not in evidence. Just for the record, because --

MS. BOLTON: No. Is it a 501(c)(3), that's all I'm asking him.

MR. VAN HORN: Oh.

MS. BOLTON: Under technical terms. I'm not asking whether he made a profit or not. I'm asking how he incorporated himself.

MR. VAN HORN: Okay. Well, I was confused. I thought, I thought -- my confusion was the difference between filing an assumed name filing.

MS. BOLTON: No, no. I'm just asking --

MR. VAN HORN: You're asking whether it's a not-for-profit corporation.

MS. BOLTON: Yes.

MR. VAN HORN: Okay. I was confused.

THE WITNESS: The only filing is this piece of paper. If that doesn't say, then we don't know.

BY MS. BOLTON:

Q. All right. And did you ever have any employees at Gemtronics?

A. No.

Q. And you mentioned that Gemtronics did not have a bank account under --

A. Gemtronics, Inc.

Q. Gemtronics Inc. never had a bank account?

A. No.

Q. The monies that you -- the monies that you obtained from your transactions in selling the supplements, did you isolate them in a separate account or were they intermingled with your personal funds?

A. They went into an account that was called Gemtronics.

Q. And it was not a corporate account?

A. No.

Q. And is that the same account that you listed in your Answers to Interrogatories?

A. Uh-huh (affirmative).

MS. BOLTON: Okay.

EXAMINATION

BY MR. VAN HORN:

Q. So it's a -- you've been operating Gemtronics by yourself; is that correct?

A. Uh-huh (affirmative).

Q. As a sole proprietor?

A. Sole proprietor.

Q. Okay. Have you ever filed any assumed name filing documents with the --

A. A what?

Q. I'm sorry. Have you ever filed a, what's called an assumed name filing document with the Register of Deeds in your county, indicating to the public that you, William Isely, are operating as sole proprietor under the name of Gemtronics?

A. No.

(Respondent's Deposition Exhibit No. 2 was marked for identification).

BY MR. VAN HORN:

Q. Okay.

A. April 17th, it was a capricious date.

Q. It's a what?

A. It's an important date. These guys were piling on by that date.

Q. Have you seen that before, the document before?

A. Yes.

Q. What is that?

A. This was a warning letter from the FDA about the Website. I presume it was part of a concerted program with the FTC, in which they warned me that this Website -- they call it my Website.

Q. What Website?

A. They say your Website.

Q. What is that Website?

A. Agaricus.net and RAAX/Agaricus.com.

Q. Okay.

A. And they are complaining about the products as being drugs, since there are therapeutic claims made for them.

Q. Okay. Now, how was this, how was this letter sent? How was this correspondence sent, according to this document?

A. I believe it was by registered mail.

Q. Okay. I think -- I'll just represent for the record on top, on the first page --

A. Oh, it says by Federal Express. Okay.

Q. Do you remember receiving this?

A. I can't remember the specific time.

Q. Do you remember if your signature was required when it was delivered?

A. I don't know.

Q. So where did you receive this?

A. Oh, I probably received it at my front door. These guys don't have an office in our town.

Q. Okay. And so -- and that letter is addressed to who?

A. William Isely, Gemtronics, Inc.

Q. And what's the address?

A. 964 Walnut Creek Road.

Q. Which we've previously established is your home

address?

A. Yes. And it was the same address that was used for registering Gemtronics, Inc., which they put on here.

Q. Okay. All right. And I guess you flipped to the second page. It directs you to contact who? What does it do, direct you to what?

A. Philip S. Campbell, the compliance officer at the FDA.

Q. Okay.

A. And because I was already involved with the FTC and had you as my counsel, I passed this letter to you, rather than contacting Philip. I've never talked to him myself.

Q. Okay. Do you remember what -- how he handled this matter?

A. Well, yes. We responded to his warning and pointed out that Agaricus was a Brazilian Website that was managed by parties other than myself.

Q. And that was done through a letter written by my office; is that correct?

A. That was a letter that was written -- that your office submitted to him.

Q. Right.

A. I believe you had some conversations with him.

Q. Okay.

A. And he responded after that with some questions about how to contact George Otto and so forth. And I had given you some information on how to, to pass on to Campbell. And he wrote another letter thanking us for our corporation. I haven't heard from him since.

MR. VAN HORN: Okay. You want -- I'm moving along.

MS. BOLTON: Keep going.

(Respondent's Deposition Exhibit No. 3 was marked for identification).

BY MR. VAN HORN:

Q. Okay. This is No. 3. Exhibit No. 3, I'm going to introduce. It's a three-page document and I've written some hand notes on the first page. But I represent this was received through discovery by the FTC. Okay. You want to take a moment just to look at that document. And what is it?

A. (Witness peruses document). You know, I've seen this recently. It's FTC Item 00195. This was the initial warnings.

Q. What's the date on it?

A. The date on it is -- letter is the 23rd of October of 2007.

Q. Okay. When did you -- do you remember when you first saw this letter?

A. I think I first saw this with material that the FTC sent us in the last month or so.

Q. Okay.

A. And it was -- I heard about this letter. And that the FTC counsel had sent this to Agaricus.net. So the letter is actually addressed to the Website. It's not addressed to me.

Q. Okay. Looking up above there, there's a -- above that area of the letter, which says who it's to and who it is from, from being the FTC, Federal Trade Commission, it looks like it's a chain of e-mails; is that correct?

A. Well, let's see.

Q. I'm going to represent -- I think it's an internal chain between people at the FTC. I don't know how relevant it is, frankly. But, again, the letter, it says it's to -- the e-mail is addressed to Agaricus.net?

A. Yes.

Q. What is your opinion as to why you never received this on October 23rd, 2007?

A. Well, I presume at that time the FTC hadn't identified me as having any connection with Agaricus.net, so they sent it to whatever they had, which would be the Website. To consider it to be a proper warning letter to me, I think, is improper because it wasn't addressed to

me. I didn't -- it wasn't sent by a method where I could give them a receipt for it, if it was meant for me. So it probably would have ended up in Brazil and they looked at it and said, what do these crazy yankees think they are doing and threw it into the wastepaper basket because they have their own regulations and laws and they are probably operating -- I don't know. They may think they are operating according to Brazilian law and that this would be presumption to tell them what to do, but --

MR. VAN HORN: This can be off the record.

(Off-record discussion).

BY MR. VAN HORN:

Q. Okay. Previously introduced, or complaint counsel previously introduced and spoke to you about their Exhibit 2.

A. Which one of those is that? I'm nearsighted.

Q. You remember when he we went through some of these?

A. This is Agaricus.net. Sure.

Q. Okay. On page two, you remember going through this document earlier today?

A. Yes.

Q. Okay. On the second page, you identified this before, but you identified the contact information for who -- for who is the administrative contact person

identified for Agaricus.net; do you remember that?

A. Yeah.

Q. Okay. Administrative contact here; right? On the first page of complaint counsel's Exhibit 2. And then continues here; right?

A. Uh-huh (affirmative).

Q. On the second page -- and according to this document, the administrative contact person is who or what persons in this case?

A. William Isely, misspelled, and George Otto, both of us living at 964 Walnut Creek Road in Franklin, with the wrong telephone number.

Q. Why is it wrong?

A. Well --

Q. Is it close to your phone number?

A. It is close?

Q. Close, but it's not. So it appears someone attempted to put your phone number down?

A. And also to George Otto's e-mail.

Q. What is that?

A. What is that?

Q. What's his e-mail address?

A. George Otto at Takesun.com.

Q. No, it's not.

A. Sorry. G Otto.

Q. Okay. So if the e-mail contact for Agaricus.net is G Otto, just like you represented, and like this document says, do you think that's why you may have not received it, received Exhibit 3?

A. Well, see, www. Agaricus.net is not an e-mail address.

Q. I understand.

A. So I don't know where it went. See, to have an e-mail address, you have to have some name with an @. And you would leave off the www. So I don't know how it was delivered to them from this documentation.

Q. Okay. But repeating ourselves, you did not receive this documentation?

A. No.

Q. Until when?

A. I don't think -- I think you were supposed to have it in your office sometime this year, but I don't think I saw it until it showed up with this FTC number on the bottom, which was in the last month.

Q. Okay. Okay.

A. Can I make a comment on it?

Q. Certainly.

A. Well, I think it's quite relevant on the last page that the writer of this document was in a quandry as to whether they had jurisdiction. Because it says, If

you are not located in the United States -- which maybe they didn't know at the time -- we have referred the claims on your Website to the Consumer Protection Enforcement Agency that has jurisdiction in your locale. So at the time, at least, this warning letter was written, they didn't know if they had jurisdiction or not. I don't know if they have ever established it or not. Have you? Well, I can't ask her.

Q. You can do that in the parking lot.

A. I'm the only one that can answer questions.

(Respondent's Deposition Exhibit No. 4 was marked for identification).

BY MR. VAN HORN:

Q. You want to take a look at that?

A. Yes.

Q. Have you seen that before?

A. I think I saw it when you -- I think you dropped this off, got this off the Website for trademarks and sent it to me.

Q. Yeah. I'll represent that that came from the Website for the U.S. Patent and Trademark Office.

A. And you showed it to me --

Q. Okay.

A. -- I think the first time we met.

Q. Okay. What -- the trademark appears to be RAAX,

that we've discussed, and capital R, cap A, cap A, cap X, and the number 11.

A. Uh-huh (affirmative). And I think actually, the actual trademark has to also specify colors used in various areas.

Q. Well, let's see if it does.

A. Here. The color red letters on the yellow background is claimed as a feature of the mark.

Q. And that trademark, that's put on the bottles of RAAX that are manufactured or at least distributed by Takesun; is that correct?

A. Uh-huh (affirmative).

Q. Takesun being Takesun do Brasil?

A. Uh-huh (affirmative).

Q. Owned and operated by George Otto; is that correct?

A. To the best of my knowledge, yes.

Q. Okay. But this, the trademark represented in this Exhibit 4, which the Exhibit 4 states it's a valid trademark, recognized by U.S. Trademark or U.S. Patent and Trademark Office. That trademark, does it say who the owner is on here?

A. Oh, applicant is one of Takesun's branches. This one is Takesun Portugal, LDA. And he also lists a German company, that's his European business, I guess.

Q. Okay. But that's the same mark or the same, same font, same writing that's found on the bottles of RAAX that you --

A. Uh-huh (affirmative).

Q. -- have purchased from Takesun do Brasil; is that correct?

A. Uh-huh (affirmative). That's correct.

Q. I want to go back a little bit, if you can go back to when Barbara Bolton was asking you questions about the purchases made by her office or undercover agents from her office. And she introduced some envelopes. And from -- they were sent by you, according to your testimony, in response to an order for bottles of RAAX. Do you remember that testimony and that line of questioning?

A. Uh-huh (affirmative). Yes.

Q. And if I remember correctly, it was -- those products were paid for through PayPal, Inc.; is that correct?

A. They were, they were paid to the Website.

Q. Okay. Paid to the Website. What Website?

A. Agaricus.net.

Q. Okay. Were they done so by PayPal?

A. Yes. And the PayPal, I think it's Takesun.com's account that accepted the payment --

Q. Well, let's --

A. -- in one case, and the other case I think it was to one of the European branches that took the money.

Q. Okay. Well, I'm going to introduce this four-page exhibit and it's related to one of the purchases. --

A. Uh-huh (affirmative).

Q. -- made by someone identified as Riece, is it Miles?

MS. BOLTON: Miles.

Q. Whose name we saw on one of the envelopes that you had mailed out.

A. Uh-huh (affirmative). Right.

Q. So going back to that -- what did you want to say? Did you want to say something?

A. Well, that documentation shows that --

Q. Hold on. The one that I'm introducing?

A. Yeah.

Q. Hold on. Let's get it stamped, then we'll get you to look at it.

A. What do you want me to say? What's the question you want me to answer about it?

Q. I'm just going to ask you about it. I don't know. I want you to look at that document.

A. Oh, okay.

Q. Tell me what you know about it. I want to understand how this PayPal thing works.

A. I haven't seen this document until it was produced by FTC.

Q. Okay.

A. But PayPal is a method of transferring --

Q. Hold on. Let her put that sticker on there. You don't need to tell me -- tell me what PayPal is. Frankly, I don't know how it works.

A. There's been a problem with International trade of sending money back and forth.

(Respondent's Deposition Exhibit No. 5 was marked for identification).

BY MR. VAN HORN:

Q. Okay.

A. In the olden days it was done by going down to your bank and sending a wire transfer. It might take half an hour or two hours, depending on where your bank was and how you got waited on. Actually, this is a way I paid for most of my purchases.

But this guy in California came up with a scheme where he would hold the money on the Internet. And people would -- got where they would trust him. So you would pay into his account and he would transfer that money to who you say you want it to go to.

So you'd have -- anyone around the world can become a member in PayPal. And this got around to banking regulations and money importing and made Internet commerce much more feasible. And so a lot of people that work on -- particularly people who are in countries that have very strict control on financial transfers, they can maintain a PayPal account in Germany, live in Brazil, and that money never comes to Brazil.

Q. Oh, okay.

A. Now they can accept it in Germany and send it to Spain or something like that, and it doesn't have to go across --

Q. State lines or country lines?

A. Yeah. Yeah. And so that's, that's the kind of system that George has adopted. He didn't, he didn't have it until about four years ago. He went to -- he went back home, put his boys in school in Europe, I understand, and set up banking arrangements there so he wouldn't have to deal with the complications of Brazilian banks.

Q. Well, here's what I want to you say, is I want you to look up here at the top here.

A. Yeah. Here it says that --

Q. Well, I want to just see who this, who this payment was made to via PayPal.

A. Well, this is a receipt to Riece Miles.

Q. Okay.

A. Telling him that his payment has gone to George Otto, I mean gotto@takesun.com, 130, no, $119.90.

Q. And then -- but the product was shipped from your house on Walnut Road; right?

A. Yeah.

Q. So how -- I may be -- we may be covering old information, but how did you know to ship it to Riece?

A. Well, George, in this case, sent me an e-mail, which is not in evidence here, that he had, he had somebody he'd like me to send a bottle of RAAX to, and this was the address. And that he had received payment for it by PayPal.

Q. He said he had received payment for it by PayPal?

A. Yeah.

Q. And so you dropped it in the mail?

A. Yeah.

Q. And that's it?

A. Yeah.

(Respondent's Deposition Exhibit No. 6 was marked for identification).

BY MR. VAN HORN:

Q. Okay. Same exercise here with this next exhibit

I'm going to introduce. This is Respondent's 6. And same questions.

A. But not the same --

Q. And this is the second of the two undercover purchases. You can let counsel see that.

A. Okay.

Q. Three pages to it. Actually, I just found it. Just put them in the right order, actually.

A. All right. This is again a statement by PayPal that they have --

Q. Who is the -- I'll represent the name on there.

A. Okay.

Q. First page is it Dana Long?

A. Dana Long, who is in Roanoke Virginia.

Q. You remember the previous line of questioning related to the undercover purchases. The first person that did undercover purchase was Riece Miles; right?

A. Yes.

Q. And the second person is this person, who is --

A. Dana Long. And the second page here is a receipt from PayPal.

Q. What's it say?

A. An e-mail to Dana Long saying that they are in receipt of his payment to Takesun Portugal LDA.

Q. Okay.

A. On one of these they had a Takesun logo, but I don't see that on this one.

Q. And if you go down, that second page says business information, contact e-mail.

A. Yeah, contact is ven dos, that probably means the giver of information, at TakesunPortugal.com.

Q. Do you know who that is or what e-mail that is?

A. All I know is that TakesunPortugal.com is one of George's businesses. I one time, when he had products that had been sent to me by mistake instead of to Europe, why he had me forward them to that address or that company, Takesun Portugal.

Q. So for both those transactions, how much money did you receive of those?

A. According to my PayPal records, I never received any.

MR. VAN HORN: Okay.

MS. BOLTON: And I have a couple of follow-ups on this.

MR. VAN HORN: Sure.

EXAMINATION

BY MS. BOLTON:

Q. And do you recall whether or not you received reimbursement from Mr. Otto with regard to these orders?

A. Specifically for these, no. He has paid me on

occasions, but --

Q. All right. So you're saying, no, you don't recall or, no, you didn't receive any reimbursement from Mr. Otto?

A. For these purchases? I don't remember ever receiving anything and my PayPal records don't show that I did.

Q. Can you read this bottom line here into the record?

MR. VAN HORN: Tell them what page you're reading off of. First page?

MS. BOLTON: Off the first page.

A. I think that's an optional way of charging.

Q. Can you read it into the record, so we know what you're talking about?

A. If Dana Long had, Dana Long had selected to pay by credit card, then I would have been, I would have received his credit card number and I would have charged it.

Q. Okay.

A. So that he would -- when it showed up on his account, he would know this is the person that charged it.

Q. The record doesn't indicate what it is you're talking about, that's why I want you to read the record,

the sentence into the record.

A. Your credit card is charges using SSL secured server. On your statement will appear Gemtronics secure payments.

Q. All right. Now, explain what you just said because I'm not sure. If -- did you just say that if the person had paid for this on a credit card --

A. If he had selected to pay by credit card --

Q. Uh-huh (affirmative).

A. -- which he did not, then George had the option of asking me to collect for the money.

Q. So it would have gone to you?

A. What would have gone to me?

Q. The payment.

A. Yes.

MR. VAN HORN: All right.

THE WITNESS: In this case he selected PayPal.

MR. VAN HORN: All right. This is six pages.

THE WITNESS: I think I should put a postscript on it. I think it's perfectly fair to charge for product that I was sending. You missed part of that.

MR. VAN HORN: Yeah.

(Respondent's Deposition Exhibit No. 7 was marked for identification).

EXAMINATION

BY MR. VAN HORN:

Q. This is a -- I'll represent this is a WHOIS search result document --

A. Uh-huh (affirmative).

Q. -- that's similar to the ones we've gone through before with Ms. Bolton, when she was asking you questions. This one, however, is regarding the domain OPC Agaricus.net.

A. Uh-huh (affirmative).

MR. VAN HORN: And I don't think we -- we didn't go over that one.

MS. BOLTON: We did.

MR. VAN HORN: We did. That is has been introduced, OPC has? Good.

THE WITNESS: This is the one I had not seen before.

MS. BOLTON: Yeah, he did not know about it.

MR. VAN HORN: Let me just make sure.

MS. BOLTON: It's the last one, I think.

(Respondent's Deposition Exhibit No. 7 was stricken and another document was marked No. 7).

BY MR. VAN HORN:

Q. What is that document?

A. This document is an invoice from the Takesun company to me listing the contents of a shipment of a

number of different items.

Q. And you received that why?

A. This kind of a document is required in international trade, in order to pass through customs and the FDA. They have to list what it is. You notice it has the -- these are the, what do they call that, harmonized tariff codes. In other words, for common products like Agaricus mushrooms, for example, the world has agreed that they will use the same number to designate.

Q. Oh, I understand.

A. And like for dried mushrooms, this is the code, 0712.31.10.00. So actually when the FDA looks at what's in a package, they look at this. Only one of maybe 20 times do they actually go down and verify it. The package sits unopened in their bonded warehouse. I mean, in the bonded warehouse of the shipper company. And they just go through this document and say, yeah, we recognize what that is and it's all right to import it. This was in February of 2003.

Q. So is this, is this a good example of an invoice that you would get as a result of buying products from --

A. Well, this is the English version. Now, in order to export, he fills out a Brazilian version.

Q. Okay.

A. So both papers come in the package.

Q. Okay.

A. And they put them in a transparent envelope and paste it over the box with tape so any agent along the way wants to look at the paper can slit it open, look at it, put it back in. And this clearly shows me as a purchaser, separate from the company selling the product, Takesun. And at the time they were operating out of Ibuna SP, which is their state in Brazil, which is up near the rain forest. They have since moved away south from there. They are now in a town called Joinville.

MR. VAN HORN: Okay. That's all I have on that. Here's No. 8.

(Respondent's Deposition Exhibit No. 8 was marked for identification).

BY MR. VAN HORN:

Q. Okay. Have you seen this document before?

A. Yes.

Q. How did you come to see it or do you know -- tell us about it.

A. I believe that you got this document in response to a query to these guys Domain Discover, and I think you sent me a copy of it. This is a statement by Pablo Velasco, who is a supervisor in Domain Discover, states that -- he says, I hereby confirm that the information

listed for the domain of Agaricus.net is legitimate and listed below. It was registered to Agaricus International, BR, 101 KM, 22.5, Joinville, SC, and postal code number, Brazil, and lists the telephone number. And it's George Otto Takesun.com.BR. And the name, domain name is Agaricus.net and administrative contact, technical contact and zone contact, those are all the same as the registrant was.

Q. Okay. But in previous, in a previous document, it's Deposition Exhibit 2 introduced by Complaint counsel, these people, these titles, registrant administrative contact --

A. Yeah, they --

Q. Those -- the documents speak for themselves, but the registrant was identified as you?

A. Uh-huh (affirmative).

Q. And the administrative contact was you, identified as you and George Otto. And now this document --

A. Well, this postdates -- this date is later than that.

Q. Why do you think they are different?

A. Well, the reason it's different is I objected and they corrected it to the proper owner and the proper registrant. And in addition, they add down here, domain

created 13 June, 1998 and expires 12 June, 2009. So he's had this domain for that length of time. He just changed the registrant for whatever purpose this might have been, because he avoided taxes or something, I don't know.

Q. So back to Exhibit 2, it also says, does it not, that the domain was created June 13th, 1998?

A. Yeah.

Q. Back over here?

A. Yep. That date and this date is the same.

Q. Okay. Because we're talking about the same Website --

A. Yeah.

Q. -- or domain?

A. Yeah.

Q. When's the first time you met George Otto?

A. I never met him.

Q. Well, when did you come to know him?

A. Oh, about in the year -- well, maybe late '99 to 2000.

Q. So you met him, first spoke with him on the Internet --

A. Yeah.

Q. -- after this domain was created?

A. Yeah.

MR. VAN HORN: Okay.

MS. BOLTON: I'd like to have a couple follow-up questions.

MR. VAN HORN: Sure.

EXAMINATION

BY MS. BOLTON:

Q. If you met him after this domain was created, how do you think your name got on it?

MR. VAN HORN: I think he just testified to that. Just said that they -- he switches them from time to time. But go ahead.

A. I'll give you his explanation and I'll tell you what I think really happened. His explanation is that at the time he created Our-Agaricus.com, he had just created that new domain for me in June of 2004. And when you create -- when you're doing business at one of these domains, one of the things they do before you sign off is they ask you, is there any other domain that you would like to renew, because they are always trying to get business.

And he realized that he had these three domains that were about to, rent was about to run out, and so while he was still in the account that he had created for me, he then put in the names of these other domains that he wanted renewed. And the computer automatically picked up the account information that he had inserted for my

domain and attached them to all of his.

Now, that's his explanation. But then why did it happen again 2006? One of his newer domains that didn't exist in 2004, in 2006, also had my name attached to it. And so the only thing I can come up with is that Brazil is a very corrupt country where everything requires a gift.

MR. VAN HORN: Right.

A. And there's taxes on everything and there's probably some way of saving money by having these domains registered outside of the country. And when I called him on it, why he promptly changed it.

Q. And I want to point out for the record that this, this Pablo Velasquez letter, which is the Respondent's last exhibit, is undated.

Secondly, it also says that it was -- that it records that the last updated date for the domain is April 15th, 2008.

Mr. Isely, would you speculate that this was updated after you contacted Mr. Otto?

A. Yes. I contacted, I contacted him immediately after I received your information from you. I was pretty blunt with him that I considered it in a category of identity theft and expected him to correct it immediately. So I'm sure that's why it happened then.

MS. BOLTON: I'm done.

MR. VAN HORN: And just for the record, there is a -- this is an attachment to an e-mail. And I will get you the transmittal e-mail with that.

MS. BOLTON: Okay.

MR. VAN HORN: So I'll clear up that date issue.

EXAMINATION

BY MR. VAN HORN:

Q. Did you have -- well, you were looking at those interrogatories earlier. Do you have those in front of you? I just want to clear up a couple things, Bill. You remember we replied to FTC's interrogatories?

A. Yes.

MS. BOLTON: You want this on the record?

MR. VAN HORN: Yeah. It is on.

Q. This is our answer here. This is number five, interrogatory number five. Okay. I'm just giving you some background. Interrogatory number five, she asked you a series of questions or a question and we responded. And the question was, how many, total amount of sales of RAAX --

A. Uh-huh (affirmative).

Q. -- bottles. And you broke it down. And she asked from '04 to the present. Question speaks for itself. But -- so you provided the information for the

year '04 through '08. And the numbers -- the total bottles sold here, if you add these up, is 918 bottles. I'll just represent that to be the case. Barbara added those up earlier.

A. Uh-huh (affirmative).

Q. Okay.

A. So I'm off in my counting somewhere.

Q. Well, yeah. If you continue down to your answer, total bottles sold is 1,134. Is there any reason that that's different? I mean, I -- maybe it's just like you say, an accounting error, but can you explain that?

A. I can't explain it at the moment.

Q. Okay. That's fine. Okay. Gross sales estimates, I'm going back to answer number five, year '04 was 7,200; '05 was 4,400; for year 2006 was 17,640; year 2007 was 26,880; 2008 is 18,960. Those are gross sales estimates; is that correct? That's what you indicate on here. That's what it states.

A. Yeah, that's before expenses and profit and so forth.

Q. Okay.

A. I mean, I mean --

Q. No, I understand. It's gross.

A. I didn't make -- I didn't mean profit on that. I mean fixed expenses.

Q. Sure.

A. It's not net profit. No, that's gross sales. In other words, that is basically taking -- well, the first year RAAX was quite expensive and it was declining in price and I estimated an average bottle cost $400. And so after that I pretty well leveled out on a price of $120 a bottle. So I -- that's why I called it an estimate, because I really counted the bottles. I didn't add up, when I came up with this, I didn't add up with every sale because it would be kind of hard to do, because you'd have to pull out the RAAX from everything else that was sold.

Q. But the way this has been answered here, this is -- these gross sale estimates are for RAAX?

A. Yes, only RAAX.

Q. Okay. So the gross sales estimate -- so this number does not include subtracting what you had to pay --

A. Oh, no.

Q. -- to George Otto --

A. No.

Q. -- to buy the product?

A. No.

Q. Okay. So your net on there -- I mean, I know you don't have your number or your books in front of you,

but what do you think your net profit is for '04?

A. Net profit?

Q. I mean --

A. I had priced it --

Q. -- estimate.

A. -- after my first year's experience, so that my gross profit, take the difference between what I paid for a product and sold it for was ranging around 25 percent. And by the time I took my expenses and shipping, importing and things like that, it came out to about a 10 percent net profit, which was -- but was carried through on my income taxes.

Q. So the, I guess -- yeah, your net income includes Social Security and you say you have a pension or something?

A. No, my net income for this item?

Q. Right. But I'm saying, what do you think that is?

A. 10 percent of that.

Q. Okay. $720. And would you, would you think about the same, 10 percent each year?

A. Uh-huh (affirmative).

Q. So the year 2005, 440; 2006, whatever that is, 1,164; 6,880, 8,000 -- 1,800. Okay.

Okay. So for each year you'd say your net is

probably 10 percent; is that right?

A. Yeah.

Q. Okay. Let me ask you what -- since this action was initiated, what steps have you done to cease doing business? You testified earlier that you're no longer -- you're not in the dietary supplement business at all any more; is that correct?

A. Yes, that's correct. I have closed out my sales tax account with the state. I don't have any inventory. I stopped importing. Last order was the one that I said was held up by the EPA, because it didn't identify the type of preservative. And I think I took delivery on that in about July time period. And so I have no inventory to sell and -- well, I've got that bottle. But I don't want to sell it, because I might need it as a sample. I'm supposed to -- I think one of your directives said, if I came to a hearing, I should bring a sample of my product. So I'm saving that one.

Q. All right. So your -- so you've ceased -- not only have you ceased selling RAAX, you've ceased selling any dietary supplemental products; is that right?

A. (Nods head affirmatively). Yeah. Actually, one of the reasons I did that is my name is poisonous to some of these people that might buy from me, the concern that they might have a similar experience.

Q. I got you.

A. But I don't have any customers.

MR. VAN HORN: Let's see. All right. I think that's all the questions I have.

(Deposition concluded at 2:52 p.m.)

CERTIFICATION OF REPORTER

DOCKET/FILE NUMBER: 9330

CASE TITLE: GEMTRONICS, INC., and WILLIAM H. ISELY

I, HEREBY CERTIFY that the transcript contained herein is a full and accurate transcript of the notes taken by me at the hearing on the above cause before the FEDERAL TRADE COMMISSION to the best of my knowledge and belief.

DATED: February 11, 2009

_____

MARY K. HUTH-STEPP, RPR
Notary Public Number 20042390053
State of North Carolina

CERTIFICATE OF DEPONENT

I hereby certify that I have read and examined the foregoing transcript, and the same is a true and accurate record of the testimony given by me.

Any additions or corrections that I feel are necessary, I will attach on a separate sheet of paper to the original transcript.

_____

WILLIAM H. ISELY

I hereby certify that the individual representing himself to be the above-named individual, appeared before me this

_____day of_____,_____, and executed the above certificate in my presence.

_____

Notary Public

My Commission Expires:_____

WITNESS: WILLIAM H. ISELY
DATE: FEBRUARY 4, 2009
CASE: GEMTRONICS, INC., ET AL.

Please note any errors and the corrections thereof on this errata sheet. The rules require a reason for any change or correction. It may be general such as, "To correct stenographic error," or, "To clarify the record," or, "To conform with the facts."

PAGE	LINE	CORRECTION	REASON FOR CHANGE

WHOIS Search Results for: OUR-AGARICUS.COM

The data contained in this Registrar's WHOIS database,
while believed by the registrar to be reliable, is provided "as is"
with no guarantee or warranties regarding its accuracy. This
information is provided for the sole purpose of assisting you
in obtaining information about domain name registration records.
Any use of this data for any other purpose is expressly forbidden without the prior written
permission of this registrar. By submitting an inquiry,
you agree to these terms of usage and limitations of warranty. In particular,
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purpose, such as the transmission of unsolicited advertising and
solicitations of any kind, including spam. You further agree
not to use this data to enable high volume, automated or robotic electronic
processes designed to collect or compile this data for any purpose,
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Please note: the registrant of the domain name is specified
in the "registrant" field. In most cases, the Registrar
is not the registrant of domain names listed in this database.

Registrant:
William Isely
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States

Registered through: Cheap-DomainRegistration.com
Domain Name: OUR-AGARICUS.COM
Created on: 01-Jul-04
Expires on: 01-Jul-08
Last Updated on: 31-Mar-08

Administrative Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
8283697590

Technical Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
8283697590

Domain servers in listed order:
NS35.DOMAINCONTROL.COM
NS36.DOMAINCONTROL.COM

Registry Status: clientDeleteProhibited
Registry Status: clientRenewProhibited
Registry Status: clientTransferProhibited
Registry Status: clientUpdateProhibited

See Underlying Registry Data
Report Invalid Whois

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Corp. 1
N. ISELY 2/10/09
PENGAD 800-631-6989

00005

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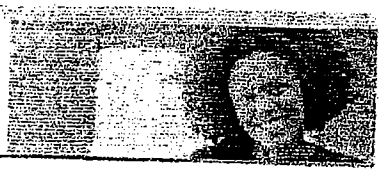


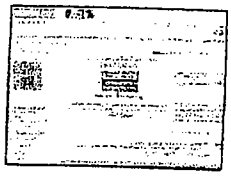
WHOIS Search Results

Available agaricus extensions:

.tv	.bz
☐	☐

Order Selected Domain(s)

Your WHOIS Search Results



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Registrant:
William Isley
964 Walnut Creek Rd
Franklin, NC 28734-9533
US

Domain Name: AGARICUS.NET

Administrative Contact, Technical Contact, Zone Contact:

DEPOSITION EXHIBIT
PENGAD 800-631-6989
Comp. 2
W. Isley 2/4/09

00028

William Isley
George Otto
964 Walnut Creek Rd
Franklin, NC 28734-9533
US
(828)389-7590
gotto@lakesun.com

Domain created on 13-Jun-1998
Domain expires on 12-Jun-2008
Last updated on 26-Nov-2007

Domain servers in listed order:

DNS1.SUPREMEDNS.COM
DNS2.SUPREMEDNS.COM

The previous information has been obtained either directly from the registrant or a registrar of the domain name other than Network Solutions. Network Solutions, therefore, does not guarantee its accuracy or completeness.

Show underlying registry data for this record

Current Registrar:	DOMAINDISCOVER
IP Address:	209.25.170.23 (ARIN & RIPE IP search)
IP Location:	UK(UNITED KINGDOM)
Record Type:	Domain Name
Server Type:	Apache 2
Lock Status:	clientTransferProhibited
Web Site Status:	Active
DMOZ	1 listings
Y! Directory:	see listings
Web Site Title:	~Agaricus blazei Murill - Alternative Therapies
Meta Keywords:	Agaricus blazei Murill, Mushrooms Alternative Cancer Therapies, HIV, Free Visits, Icacop filaume,Chrysobalanus icaco <meta name=
Secure:	No
E-commerce:	No
Traffic Ranking:	Not available
Data as of:	13-Sep-2005

Search

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Search

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Go

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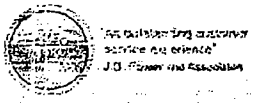
Go



100% Secure Transaction

For your protection, this Web site is secured with the highest level of SSL Certificate encryption.

00030

Agaricus Net

Best Price/Best Quality

Not working Chemo ..and now..

OPC Agaricus Protocol ..try it

Cannot find your XML file. You need to upload it for this form to work.

Specially at breast cancer the OPC Agaricus protocol shows that it works in

99,9% of all cases. Even at late stage IV it seems to work. From late 2004 to today about 5217 women took the protocol. Many doctors all over the world are, reporting, since he is using the OPC Agaricus protocol nobody of his patient died. So we receive this positive message everyday from all over the world. Now many, many patients entered into the protocol from UK, where many clinics started to use our special protocol.

If you are living in the US, just call Mr. Isely and he will explain how it works. Or fill out form

* Required

(Explanation)

Has a cancer killer been discovered?

RAAX11 Extract FDA registered *

Brazilian scientists have discovered a tropical plant substance that holds greatpromise in the fight against various types of cancer. Up to now, this South American folk remedy has mainly been used against diabetes.

Scientists report that during laboratory tests the substance destroyed cancer cells that had been resistant to treatment up to now. This is a rare occurrence. The substance is so promising it is being kept under wraps at present. **Even very resistant Leukemia cells die off Informations USA 828-369-7590 or Brazil 55 47 3001.5260 or UK 44 020 8133 2774**

Cancer and no hope

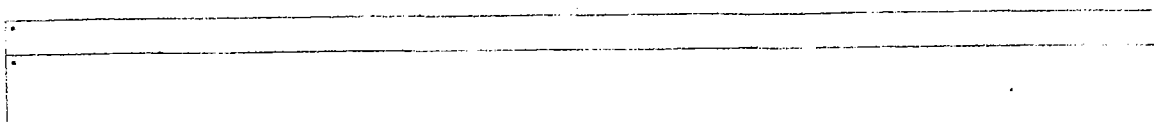
You need help?

Let's talk about it...

Anti cancer effect: ABM contains natural steroids, known for it's anti cancer effect. (It is different from the chemically produced steroids that enhance the body that is often said to be the cause of cancer). It is particularly effective in prevention of uteran cancer.

* Manufacture is FDA registered

Exhibit A



Agaricus Net

Best Price/Best Quality

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Lung Cancer
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Home

Agaricus blazei Murill from Brazil

Breast Cancer Patients in remission (2006)
621 out of 749 People in remission taking
the RAAX11 protocol:

1) B.S Canada - 04.2006 (started IV)
2) S.R Canada - 05.2006 (started IV)
3) F.B China - 05.2006 (started IV)
4) A.H. Hong Kong - 05.2006 (started IV)
5) D.F. Macau - 05.2006 (started IV)
6) A.S. Germany -05.2006 (started IV)
7) V.T. UK - 06.2006 (started IV)
8) T.U. Norway - 06.2006 (started III)
9) J.R. Spain - 06.2006 (started IV)
10) R.L. Australia 06.2006 (started II)
11) B.W. USA 06.2006 (started IV)
12) L.A. USA 07.2006 (started IV)
13) F.G. USA 07.2006 (started III)
14) H.L. USA 07.2006 (started IV)
15) U.L. USA 07.2006 (started IV)
16) V.S. USA 07.2006 (started III)
17) J.S. UK 07.2006 (started IV)
...ect....

Contact:
Intl. Tel.xx1 828-369-7590
US Tel. (free) 866-944-7359
FAX. 828-369-5861

RAAX11 Offers New Hope for an Alternative Breast Cancer Treatment

In a recent study, 91 women who were suffering from breast cancer at stage IIIb or IV took part in our RAAX11 protocol. By April 2004, 41 women had totally recovered, 23 women were in remission, 27 were stable, and only 9 had not survived, a survival rate of 91.27%. If you would like to find out how you too can participate in our ongoing study in the USA , call 828-369-7590

History

tested very positive with other forms of cancer, and. In 2003 we later developed a new formula with even stronger rainforest herbs for women who had been diagnosed as hopeless. That product is our RAAXX11.
In 2004 we began a trial with 91 women who were suffering from breast cancer and were diagnosed as either stage IIIb or stage IV, and who decided not to participate in a program of chemotherapy or use some other chemical therapy. These women began following a natural Agaricus program, where the Agaricus extract RF1000 was mainly used. By April, we had received confirmation that 3 women were 100% cancer free. That same month we added the new RAAX11 extract to the RF1000 protocol. Here are the results so far:

Results:
41 Patients, entered with stage IV/IIIb, taking RAAX11 plus RF 1000, are in total recovered.
23 patients, entered with stage IV/IIIb, taking RAAX11 plus RF 1000, are in remission.
27 Patients, entered with stage IV/IIIb, taking RAAX11, plus RF 1000, are in the same stage, no change.
9 Patients, entered with stage IV/IIIb, taking RAAX11, plus RF 1000, did not survive treatment.

These figures show an extremely encouraging survival rate during our trial of 91.27%. We are proud to say that our new program may offer hope for women who are looking for alternatives.

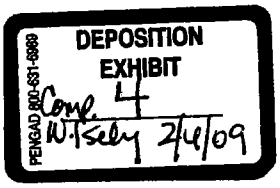

Exhibit C

For personal reasons, in 1999 we began to try to develop a natural alternative to help women with breast cancer whose only choice seemed to be chemotherapy. So we developed the RF1000 protocol, which also

If you are interested in this program, feel free to contact us and we will set you up with an alternative clinic.

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To:/Destinataire:
Riece Miles
Lorton, VA 22079
Country of Destination:/Pays de destination:
U.S. POSTAGE PAID FRANKLIN, NC 28734 JAN 10 '08 AMOUNT $7.20
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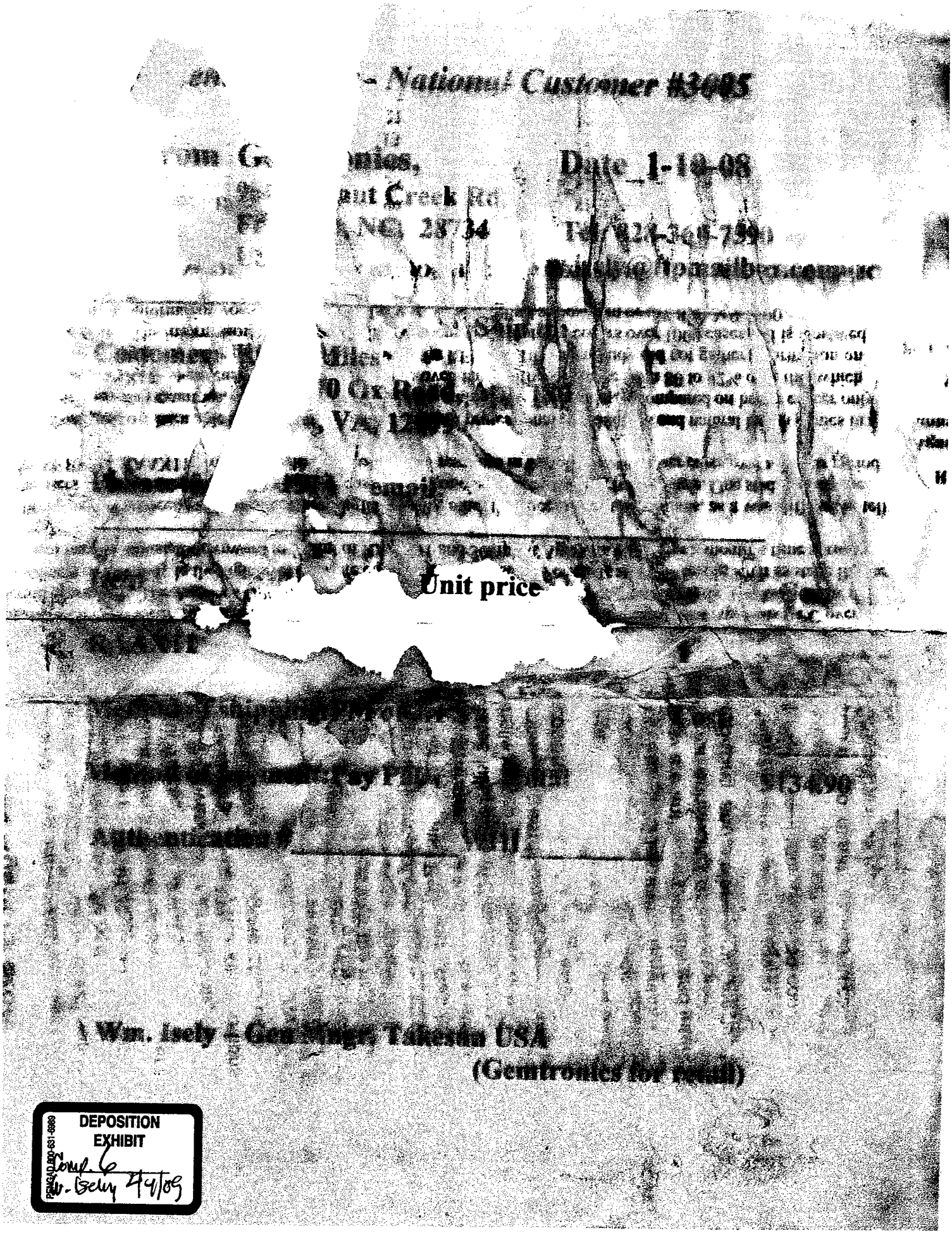
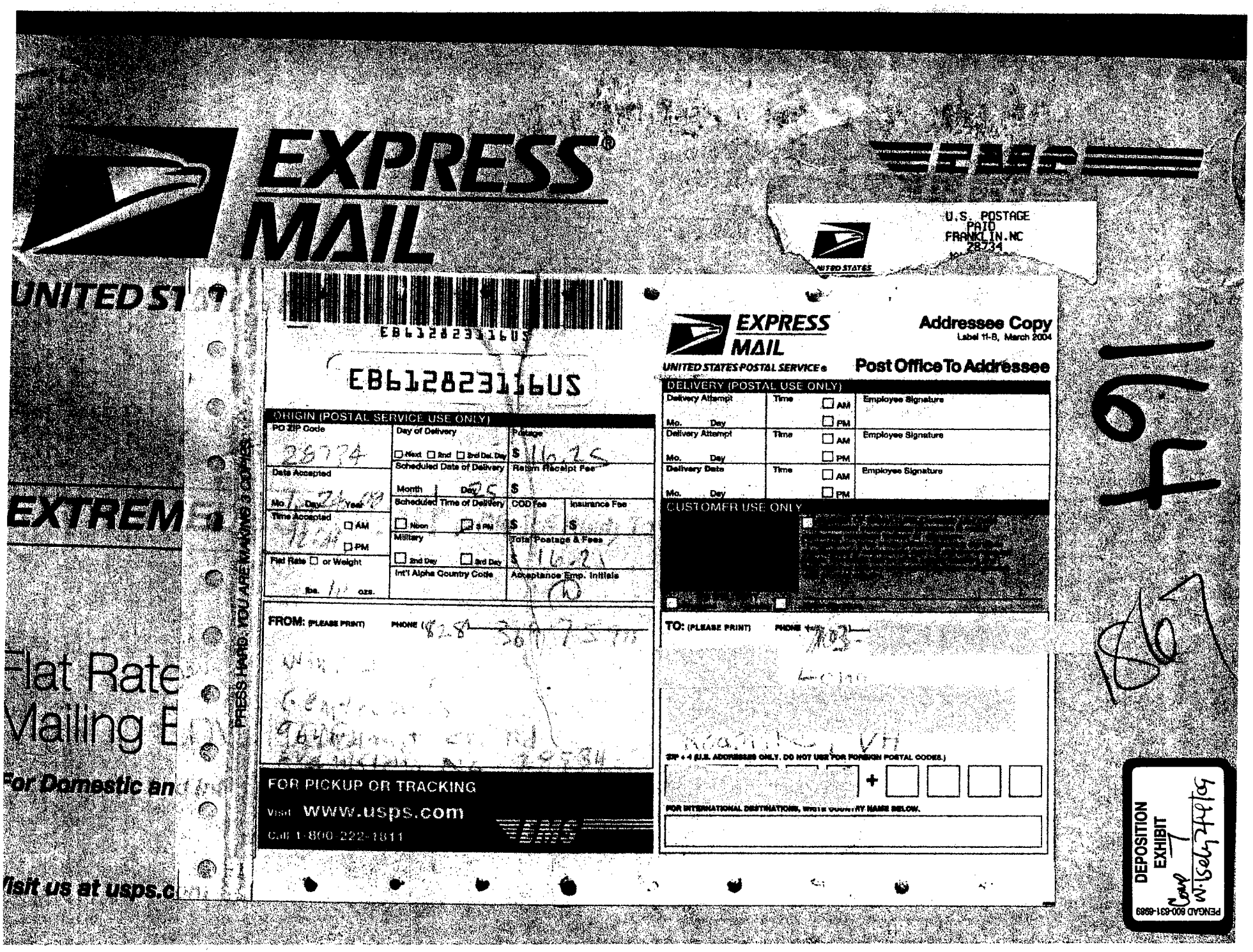
W. Ieely 2/4/09



DEPOSITION EXHIBIT
Count 6
Wm. Isely 4/4/09


EXPRESS MAIL
U.S. POSTAGE
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28734
UNITED STATES
EB612823116US
EXPRESS MAIL
UNITED STATES POSTAL SERVICE
Addressee Copy
Label 11-B, March 2004
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ORIGIN (POSTAL SERVICE USE ONLY)
PO ZIP Code
28734
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Postage
Date Accepted
Scheduled Date of Delivery
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Time Accepted
Scheduled Time of Delivery
COD Fee
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Delivery Attempt
Time
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Shipment Invoice - National Customer #3019

From Gemtronics, **Date_1-24-08**

964 Walnut Creek Rd.
Franklin, NC, 28734 **Tel: 828-369-7590**
USA **w.isely@ftpmailbox.com**

Ship to:

Customer: Dana Long
[redacted]
Roanoke, VA, 24018

Phone:703-[redacted] **email:**

Item	Unit price	No	Cost
RAAX11	$119	1	$119
Method Of Ship: UPS	shipping & Handling	Cost:	15
Method of payment: Pay Pal		Total	$134

Authentication #_____WHI_____

Note: Please order direct by phone or email in the future.

Thanks, Bill Isely

OPC
500ml - new

Camu Camu
120 Caps $15

The Agaricus blazei Murill Mushrooms are grown in their natural location free of any contaminants, dried so as to conserve their important nutrients of which Beta Glucan is critical for strengthening the immune system.

Takesun do Brasil

Then packages the mushrooms in various ways: dried, powder, extracts, capsules, and also in combination with other rain forest herbs for exporting to many countries around the world.

For more information go to web site:

Go to www.agaricus.net
Click on USA sales. or
www.our--agaricus.com

Gemtronics
Tel: 828-369-7590
Email:w.isely@ftpmailbox.com

The Agaricus Story

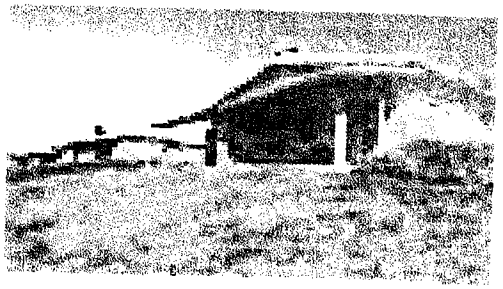
Some years ago a Japanese researcher In the Piedade section of Brazil noticed that the native people of the rain forest who used the Agaricus blazei Murill mushrooms as part of their diet were much healthier than the westerners who ate a conventional diet. He noticed that they were particularly free of conditions that we today call degenerative ones.

Samples of the mushrooms were sent to Japan where the mushrooms were seen to have beneficial effects which were attributed to the fact that the mushrooms were found to have the highest known natural source of beta glucan, among other nutrients. Beta glucan has long been known as a substance that stimulates killer cells of the immune system, cells very critical to the ability of the immune system to handle degenerative conditions.

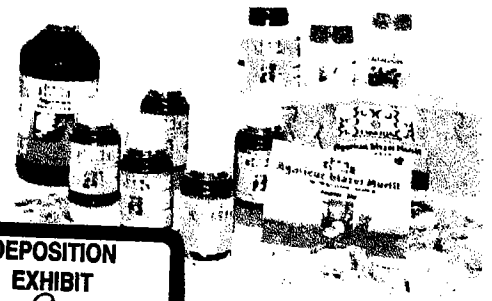
Agaricus blazei Murill mushrooms were found to have other beneficial properties as well. Besides immune enhancing, they are anti-tumor, interferon and interleukin enhancing, anti-viral, cholesterol reducing, and a blood sugar modulator.

Agaricus has also been found valuable for certain conditions when combined with other rain forest herbs: cat's claw, pau d'arco, mutamba,. camu camu, and Chrysobalanus Icaco.

TAKESUN® U.S.A.



Agaricus Mushroom Products From The Rain Forest



RAAX11 / AGARICUS OPC PROTOCOL DESCRIPTION AND RESULTS

Takesun has been developing various Amazon Rain Forest derived liquid extract blends, all involving the Agaricus brazei Murill mushroom, principally for support of combating various degenerative health conditions. The RAAX11 / Agaricus OPC protocol for stage IV conditions is the taking of 500ml of RAAX11 and 1000ml Agaricus OPC over a period of a month. The Agaricus OPC part is gradually introduced over a period of a month to six weeks to allow the adjustment of the body to the high level of waste elimination that results. For cases at lower levels, such as stage II, the protocol may be adjusted downward to 300ml of RAAX11 and 500ml of Agaricus OPC over a month's time period.

In the past it has been hard to collect meaningful results, other than occasional testimonials, as it was difficult to tell if the users followed the protocols and in most cases were not observed by health professionals. One study, using the older RF1000 / RAAX11 protocol, yielded a successful response in 80% of breast cancer cases over a 1 year period.

Takesun has now been able to gather meaningful data from professional practitioners and natural health clinics in a number of European countries, Germany, the UK, Austria, and Spain. The results, if compared on breast cancer only, are that the RAAX11 / Agaricus OPC protocol has improved the positive response from 80 to 92% over that which was demonstrated by the older protocol, RAAX11 with the RF1000. The older study did not gather information on other conditions. The information on the RAAX11 / Agaricus OPC protocol covers over 1000 cases and is tabulated below. For more information contact William H. Isely at w.isely@ftpmailbox.com or call 828-369-7590.

CONDITION	No. OF CASES	No. RESPONDING	% RESPONDING	% NOT RESPONDING
Lung	413	321	78	22
Gastro	122	99	81	19
Intestinal	55	35	64	36
Larynx	21	9	43	57
Esophagus	25	13	52	48
Brain	29	21	72	28
Lymphatic	5	3	60	40
Breast	371	342	92	8
Leukemia	41	32	78	22
Sarcoma	4	3	75	25
Thyroid	5	4	80	20
Prostate	76	65	86	14

While the lifestyles of these individuals are not known, it is assumed that they represented a cross-section of Europeans. Someone on the protocol also going onto a Mediterranean diet, avoiding most meat, using organic sources as well as using good supplements, including anti-oxidents, could reasonably expect an even better outcome.

RAAX11 - 100ml

(Agaricus and Chrysobalanus Icaco)

$119 Each

Protocol - 5 bottles/month

Agaricus OPC - 500ml

(Agaricus, Nerium Oleander, Pau d'Arco, and Cat's Claw)

$130 Each

Protocol - 2 bottles/month

--- POPULAR PRODUCTS ---

Agaricus Blazei Murill Mushrooms 100 g, Grade A $25 Golden $29.90

Normally packed in an air-tight bag for long-term preservation, the mushrooms can be soaked and cooked before eating or just soaked and cooked and the water then poured off to drink as a tea for therapeutic purposes.

The active constituents are Beta Glucan (1-3-3 glucan) and Ergoaterol (rovitamin D2) derivatives.

Agaricus blazei Murill Powder

100 gram bag

For those making large quantities of tea, mainly for therapeutic purposes, the mushroom powder is available as the most economical form to take the Agaricus mushroom. For best results, Agaricus should be taken with about 6,000 mg of vitamin C every day, which can be in the form of Camu Camu. For good health it is also recommended to keep the body on the alkaline side.

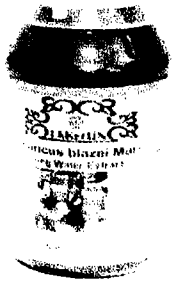
Agaricus Blazei Murill $12 Capsules

60 Capsules, 500 mg.

The capsules are commonly used for preventative purposes, similarly to taking vitamins. Usually several capsules are opened into a cup of hot water to make a tea.

Extracts For Therapy Purposes

Agaricus and blends of it with other rain forest herbs in the extract form are what are usually used for therapy purposes.



Agaricus Blazei$ 25 Murill Extract

100 ml.

Many Westerners consider the making of the tea each day to be an inconvenience and prefer to take their Agaricus in the form of an extract. A 25:1 extract Is available so that the tea can be made by adding 5 ml (1 teaspoon) of the extract to a cup of water or other drink.

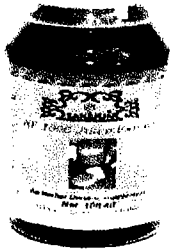
Depending on their status, people who take the extract for therapy reasons may use up to ten bottles of it in a month. For preventative purposes, people normally will use one bottle a month.

RAAX11 An extract Blend of Chrysobalanus Icaco & Agaricus - 100 ml $119

For some conditions, the Agaricus works best when it is combined with other herbs. The RF 1000 is a combination with Cat's Claw and Pau d'Arco. .

RF 1000 Extract

100 ml. **$25**

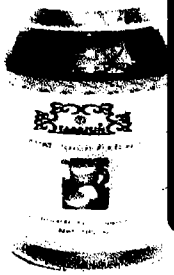


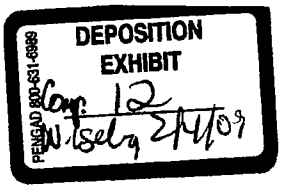
As with the Agaricus powder, a liquid extract is available in the RF 1000 for those who prefer to use the liquid to make a tea.

APM JUICE

100 ml. **$25**

A version of the RF 1000 extract is available in which the Cats Claw has been replaced with the herb Mutamba which is better for some conditions.





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WHOIS information for: our-agaricus.us:

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Domain ID:	D6352363-US
Sponsoring Registrar:	WILD WEST DOMAINS, INC.
Domain Status:	clientDeleteProhibited
Domain Status:	clientRenewProhibited
Domain Status:	clientTransferProhibited
Domain Status:	clientUpdateProhibited
Registrant ID:	GODA-07167987
Registrant Name:	William Isely
Registrant Organization:	Unknown
Registrant Address1:	964, Walnut Creek, RD
Registrant City:	Franklin
Registrant State/Province:	North Carolina
Registrant Postal Code:	28734
Registrant Country:	United States
Registrant Country Code:	US
Registrant Phone Number:	+1.8283697590
Registrant Email:	gotto@takesun.com
Registrant Application Purpose:	P3
Registrant Nexus Category:	C11
Administrative Contact ID:	GODA-27167987
Administrative Contact Name:	William Isely
Administrative Contact Organization:	Unknown
Administrative Contact Address1:	964, Walnut Creek, RD
Administrative Contact City:	Franklin
Administrative Contact State/Province:	North Carolina
Administrative Contact Postal Code:	28734
Administrative Contact Country:	United States
Administrative Contact Country Code:	US
Administrative Contact Phone Number:	+1.8283697590
Administrative Contact Email:	gotto@takesun.com
Administrative Contact Application Purpose:	P3
Administrative Contact Nexus Category:	C11
Billing Contact ID:	GODA-37167987
Billing Contact Name:	William Isely
Billing Contact Organization:	Unknown
Billing Contact Address1:	964, Walnut Creek, RD
Billing Contact City:	Franklin
Billing Contact State/Province:	North Carolina
Billing Contact Postal Code:	28734
Billing Contact Country:	United States
Billing Contact Country Code:	US
Billing Contact Phone Number:	+1.8283697590
Billing Contact Email:	gotto@takesun.com
Billing Contact Application Purpose:	P3
Billing Contact Nexus Category:	C11
Technical Contact ID:	GODA-17167987
Technical Contact Name:	William Isely
Technical Contact Organization:	Unknown
Technical Contact Address1:	964, Walnut Creek, RD
Technical Contact City:	Franklin
Technical Contact State/Province:	North Carolina
Technical Contact Postal Code:	28734
Technical Contact Country:	United States
Technical Contact Country Code:	US
Technical Contact Phone Number:	+1.8283697590
Technical Contact Email:	gotto@takesun.com
Technical Contact Application Purpose:	P3
Technical Contact Nexus Category:	C11
Name Server:	NS35.DOMAINCONTROL.COM

00037

Name Server:	NS36.DOMAINCONTROL.COM
Created by Registrar:	WILD WEST DOMAINS, INC.
Last Updated by Registrar:	WILD WEST DOMAINS, INC.
Domain Registration Date:	Thu Jul 01 18:27:23 GMT 2004
Domain Expiration Date:	Mon Jun 30 23:59:59 GMT 2008
Domain Last Updated Date:	Mon Mar 31 15:08:49 GMT 2008

>>>> Whois database was last updated on: Wed Apr 09 14:56:59 GMT 2008 <<<<

NeuStar, Inc., the Registry Administrator for .US, has collected this information for the WHOIS database through a .US-Accredited Registrar. This information is provided to you for informational purposes only and is designed to assist persons in determining contents of a domain name registration record in the NeuStar registry database. NeuStar makes this information available to you "as is" and does not guarantee its accuracy. By submitting a WHOIS query, you agree that you will use this data only for lawful purposes and that, under no circumstances will you use this data: (1) to allow, enable, or otherwise support the transmission of mass unsolicited, commercial advertising or solicitations via direct mail, electronic mail, or by telephone; (2) in contravention of any applicable data and privacy protection laws; or (3) to enable high volume, automated, electronic processes that apply to the registry (or its systems). Compilation, repackaging, dissemination, or other use of the WHOIS database in its entirety, or of a substantial portion thereof, is not allowed without NeuStar's prior written permission. NeuStar reserves the right to modify or change these conditions at any time without prior or subsequent notification of any kind. By executing this query, in any manner whatsoever, you agree to abide by these terms.

NOTE: FAILURE TO LOCATE A RECORD IN THE WHOIS DATABASE IS NOT INDICATIVE OF THE AVAILABILITY OF A DOMAIN NAME.

All domain names are subject to certain additional domain name registration rules. For details, please visit our site at www.whois.us.

Verio Inc. - Growing Your Business, One Click At A Time

00038

W. Isely

Internet Corporation Listing Service

ICLS.NET

Domain Name: raaxagaricus.com
Customer Number: DG158918
Notice Date: July 15, 2008

DESCRIPTION OF SERVICES	ANNUAL WEBSITE SEARCH ENGINE LISTING	
	FROM July 15, 2008 THRU July 15, 2009	
	TOTAL	$40.00
		$40.00

SUBSCRIPTION INCLUDES

DOMAIN NAME SUBMISSION TO 25 ESTABLISHED SEARCH ENGINES, QUARTERLY SEARCH ENGINE POSITION AND RANKING REPORTS FOR EIGHT KEYWORD/PHRASE LISTINGS FROM 25 MAJOR SEARCH ENGINES

INQUIRIES

E-mail: inquiries@icls.net
Website:www.icls.net

PENGAD 800-631-6989 DEPOSITION EXHIBIT Dep. 13 W. Isely 2/4/09

THIS INTERNET LISTING OFFER IS PROVIDED TO MILLIONS OF WEBSITES THROUGHOUT THE UNITED STATES TO ENHANCE THEIR WEBSITE EXPOSURE. THIS IS A SOLICITATION FOR THE ORDER OF GOODS OR SERVICES, OR BOTH, AND NOT A BILL, INVOICE, OR STATEMENT OF ACCOUNT DUE. YOU ARE UNDER NO OBLIGATION TO MAKE ANY PAYMENTS ON ACCOUNT OF THIS OFFER UNLESS YOU ACCEPT THIS OFFER.

Please make checks payable to: Internet Corporation Listing Service.

Customer Number	Listing Date	Amount	Amount Paid
DG158918	July 15, 2008	$40.00	

Payment Options

☐ 1 Year ($40.00) ☐ 2 Years ($70.00) ☐ 5 Years ($160.00)

IMPORTANT
Please provide us with your current e-mail address. Submission instructions will be sent to you when payment is processed.

E-MAIL ADDRESS: _____

Please remit payment to address on reverse side, do not staple

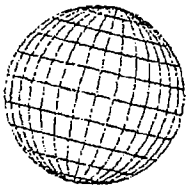
*******AUTO**3-DIGIT 287
William Isely
964 Walnut Creek Rd
Franklin, NC 28734-9533

T215 P1

THIS IS A SOLICITATION FOR THE ORDER OF GOODS OR SERVICES, OR BOTH, AND NOT A BILL, INVOICE, OR STATEMENT OF ACCOUNT DUE. YOU ARE UNDER NO OBLIGATION TO MAKE ANY PAYMENTS ON ACCOUNT OF THIS OFFER UNLESS YOU ACCEPT THIS OFFER.

00051

58918



ICLS.NET

HOW TO MAKE PAYMENT:
Please make checks payable to Internet Corporation Listing Service
Please write your customer number on the front of your check
Enclose check in the addressed envelope provided
DO NOT SEND CASH

WEBSITE ADDRESS LISTING INCLUDES:
Domain name submission to 25 established search engines
Initial and quarterly search engine positions and ranking reports sent to you via email for eight keyword/phrase listing that you select from 25 MAJOR search engines
Complete details are located on the internet at www.icls.net

PAYMENT INFORMATION:
Please remit payment on or before July 15, 2008
All listings are final

Current Payment Details

	Amount	Total
Annual Listing (July 15, 2008 to July 15, 2009)	$40.00	$40.00
Total		$40.00

Payment Information

Please make checks payable to Internet Corporation Listing Service
Please write your customer number on the front of your check
Do not send cash

Internet Corporation Listing Service
303 Park Avenue S, #1073
New York, NY 10010

00052

NetworkSolutions

Login

Customer Service
Call us toll free

Your cart is empty

WHOIS Search Results

Available **takesun** extensions:

.org	.us	.mobi	.info	.biz	.tv	.eu	.bz
☐	☐	☐	☐	☐	☐	☐	☐

Order Selected Domain(s)

Your WHOIS Search Results

IMAGE NOT AVAILABLE

takesun.com
Services from Network Solutions:

Certified Offer Service - Let us help you get this domain name!

Backorder - Try to get this name when it becomes available.

SSL Certificates - Get peace of mind with a secure certificate.

Enhanced Business Listing - Promote your business to millions of viewers for only $1 a month!

Please note: the owner of the domain name is specified in the "registrant" field.

DEPOSITION EXHIBIT
Corp. 14
Wisely 2/4/09
PENGAD 800-631-6989

In most cases, the Registrar is not the owner of domain names listed in this database.

Registrant:
George Otto
964 Walnut Creek Rd
--
,
Franklin, NC 28734

Registered through: Cheap-DomainRegistration.com
Domain Name: TAKESUN.COM
Created on: 23-Mar-00
Expires on: 23-Mar-08
Last Updated on: 09-Mar-07

Administrative Contact:
Isley, William webmaster@agaricus.net
964 Walnut Creek Rd
--
,
Franklin, NC 28734
us Fax --

Technical Contact:
, nocontactsfound@secureserver.net
,
Fax --

Domain servers in listed order:
DNS1.SUPREMESERVER20.COM
DNS2.SUPREMESERVER20.COM

The previous information has been obtained either directly from the registrant or a registrar of the domain name other than Network Solutions. Network Solutions, therefore, does not guarantee its accuracy or completeness.

Show underlying registry data for this record

Current Registrar: WILD WEST DOMAINS, INC.
IP Address: 209.25.170.23 (ARIN & RIPE IP search)
IP Location: UK(UNITED KINGDOM)
Record Type: Domain Name
Server Type: Apache 2
Lock Status: clientDeleteProhibited
Web Site Status: Active
DMOZ no listings
Y! Directory: see listings
Secure: No

E-commerce: Yes
Traffic Ranking: Not available
Data as of: 14-Jun-2005

C IP Address

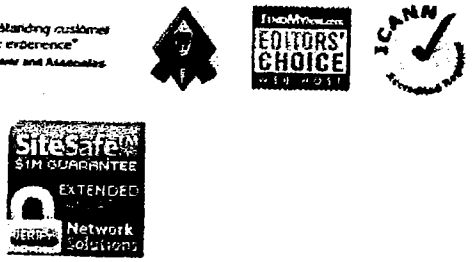
Search

Go

Need to get your business online?
Our professional designers can build a custom Web site for your business.
$11.95/month, plus a $499.00 design fee

Go

PerformanceClicks™ from Network Solutions
Create and manage your pay per click advertising from as low as **$125/month** plus **$99 one time set-up fee**



100% Secure Transaction

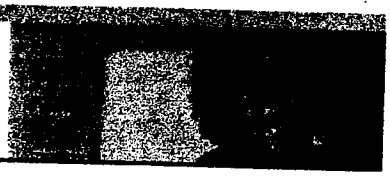
For your protection, this Web site is secured with the highest level of SSL Certificate encryption.

.NetworkSolutions

Login

Customer Service
Call us toll free

Your cart is empty



WHOIS Search Results

Available **opc-agaricus** extensions:

.com	.org	.us	.mobi	.info	.biz	.de	.tv	.co.uk	.eu	.bz
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Order Selected Domain(s) >

Your WHOIS Search Results

IMAGE NOT AVAILABLE

opc-agaricus.net
Services from Network Solutions:

Certified Offer Service - Let us help you get this domain name!
Backorder - Try to get this name when it becomes available.
SSL Certificates - Get peace of mind with a secure certificate.
Enhanced Business Listing - Promote your business to millions of viewers for only $1 a month!

The data contained in this Registrar's Whois database, while believed by the registrar to be reliable, is provided "as is" with no guarantee or warranties regarding its accuracy. This information is provided for the sole purpose of assisting you in obtaining information about domain name registration records. Any use of this data for any other purpose is expressly forbidden without the prior written permission of this registrar. By submitting an inquiry, you agree to these terms of usage and limitations of warranty. In particular, you agree not to use this data to allow, enable, or otherwise make possible, dissemination or collection of this data, in part or in its entirety, for any purpose, such as the transmission of unsolicited advertising and solicitations of any kind, including spam. You further agree not to use this data to enable high volume, automated or robotic electronic processes designed to collect or compile this data for any purpose, including mining this data for your own personal or commercial purposes.

Please note: the owner of the domain name is specified in the "registrant" field.

DEPOSITION EXHIBIT
Comp. 15
W. Isely 2/4/09
PENGAD 800-631-6989

In most cases, the Registrar is not the owner of domain names listed in this database.

Registrant:
William Isely
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States

Registered through: Cheap-DomainRegistration.com
Domain Name: OPC-AGARICUS.NET
Created on: 02-Jun-06
Expires on: 02-Jun-08
Last Updated on: 09-Mar-07

Administrative Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
(828) 369-7590 Fax --

Technical Contact:
Isely, William gotto@takesun.com
964, Walnut Creek, RD
Franklin, North Carolina 28734
United States
(828) 369-7590 Fax --

Domain servers in listed order:
DNS1.SUPREMECENTER20.COM
DNS2.SUPREMECENTER20.COM

The previous information has been obtained either directly from the registrant or a registrar of the domain name other than Network Solutions. Network Solutions, therefore, does not guarantee its accuracy or completeness.

Show underlying registry data for this record

Current Registrar: WILD WEST DOMAINS, INC.
IP Address: 209.25.170.23 (ARIN & RIPE IP search)
IP Location: UK(UNITED KINGDOM)
Record Type: Domain Name
Server Type: Apache 2
Lock Status: clientDeleteProhibited
Web Site Status: Active
DMOZ no listings
Y! Directory: see listings
Secure: No
E-commerce: No
Traffic Ranking: Not available

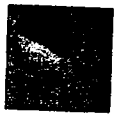
Data as of: 14-Jun-2005

IP Address

Search

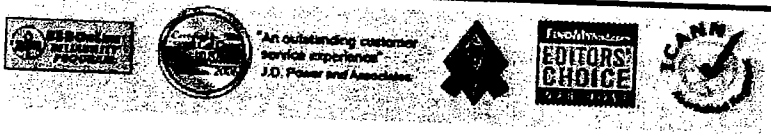
Need to get your business online?
Our professional designers can build a custom Web site for your business.
$11.95/month, plus a $499.00 design fee

Go



PerformanceClicks™ from Network Solutions
Create and manage your pay per click advertising from as low as **$125/month** plus **$99 one time set-up fee**

Go



100% Secure Transaction
For your protection, this Web site is secured with the highest level of SSL Certificate encryption.

Elaine F. Marshall
Secretary

North Carolina
DEPARTMENT OF THE SECRETARY OF STATE
PO Box 29622 Raleigh, NC 27626-0622 (919)807-2000

CORPORATIONS

- Corporations Home
- Search By Corporate Name
- Search For New Corporation
- Search By Registered Agent
- Important Notice
- Resale of Tickets Online
- Corporations FAQ
- Homeowners' Association FAQ
- Tobacco Manufacturers
- Unincorporated Non-Profits
- Dissolution Reports
- Non-Profit Reports
- Verify Certification
- Online Annual Reports

LINKS & LEGISLATION

- KBBE B2B Annual Reports
- SOSID Number Correction
- 2001 Bill Summaries
- 1999 Senate Bills
- Annual Reports 1997
- Corporations 1997
- Register for E-Procurement
- Dept. of Revenue

ONLINE ORDERS

- Start An Order
- New Payment Procedures

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- Corporations Division

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- Secretary of State Site Map
- Printable Page

Date: 1/19/2009

Click here to:

View Document Filings | Sign Up for E-Notifications | Print apre-populated Annual Report Form | Annual Report Count | File an Annual Report |

Corporation Names

Name	Name Type
NC Gemtronics, Inc.	Legal

Business Corporation Information

SOSID:	0867758
Status:	Current-Active
Date Formed:	9/20/2006
Citizenship:	Domestic
State of Inc.:	NC
Duration:	Perpetual

Registered Agent

Agent Name:	Isely, William H.
Registered Office Address:	964 Walnut Creek Road Franklin NC 28734
Registered Mailing Address:	964 Walnut Creek Road Franklin NC 28734
Principal Office Address:	964 Walnut Creek Road Franklin NC 28734
Principal Mailing Address:	964 Walnut Creek Road Franklin NC 28734

Stock

Class	Shares	No Par Value	Par Value
Common	10000	Yes	N/A

PENGAD 800-631-6989
DEPOSITION EXHIBIT
Resp. 1
W. Isely 2/4/09

00053

Elaine F. Marshall
Secretary

North Carolina
DEPARTMENT OF THE SECRETARY OF STATE

PO Box 29622 Raleigh, NC 27626-0622 (919)807-2000

CORPORATIONS

- Corporations Home
- Search By Corporate Name
- Search For New Corporation
- Search By Registered Agent
- Important Notice
- Resale of Tickets Online
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- Homeowners' Association FAQ
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- New Payment Procedures

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- Corporations Division

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Corporate Filings For: Gemtronics, Inc.

Image	Date	Document Id	Document
	9/20/2006	C200626100148	INC - Articles of Incorporation

Click here for help downloading forms.

00056

C200626100148

SOSID: 867758
Date Filed: 9/20/2006 4:21:00 PM
Elaine F. Marshall
North Carolina Secretary of State
C200626100148

State of North Carolina
Department of the Secretary of State

ARTICLES OF INCORPORATION

Pursuant to §55-2-02 of the General Statutes of North Carolina, the undersigned does hereby submit these Articles of Incorporation for the purpose of forming a business corporation.

1. The name of the corporation is: Gemtronics, Inc.

2. The number of shares the corporation is authorized to issue is: 10,000

3. These shares shall be: ***(check either a or b)***

   a. ☑ all of one class, designated as common stock; or

   b. ☐ divided into classes or series within a class as provided in the attached schedule, with the information required by N.C.G.S. Section 55-6-01.

4. The street address and county of the initial registered office of the corporation is:

   Number and Street 964 Walnut Creek Road

   City Franklin State NC Zip Code 28734 County Macon

5. The mailing address, ***if different from the street address,*** of the initial registered office is:

   Number and Street _____

   City _____ State _____ Zip Code _____ County _____

6. The name of the initial registered agent is: William H. Isely

7. Principal office information: (***must select either a or b.***)

   a. ☑ The corporation has a principal office.

   The street address and county of the principal office of the corporation is:

   Number and Street 964 Walnut Creek Road

   City Franklin State NC Zip Code 28734 County Macon

   The mailing address, ***if different from the street address***, of the principal office of the corporation is:

   Number and Street _____

   City _____ State _____ Zip Code _____ County _____

   b. ☐ The corporation does not have a principal office.

8. Any other provisions, which the corporation elects to include, are attached.

9. The name and address of each incorporator is as follows:

William H. Isely, 964 Walnut Creek Road, Franklin, NC 28734

10. These articles will be effective upon filing, unless a date and/or time is specified:

This the 4th day of Sept. 2006

William H. Isely
INCORPORATOR

William H. Isely - Agent
Type or Print Name and Title

00055

NOTES:

1. **Filing fee is $125. This document must be filed with the Secretary of State.**

CORPORATIONS DIVISION P. O. BOX 29622 RALEIGH, NC 27626-0622

(Revised January, 2002) *(Form B-01)*

FDA U.S. Food and Drug Administration

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Atlanta District Office
60 8th Street. N.E.
Atlanta, Georgia 30309

April 17, 2008

VIA FEDERAL EXPRESS

William Isely
Gemtronics Inc.
964 Walnut Creek Road
Franklin, NC 28734-9533

PENGAD 800-631-6989
DEPOSITION EXHIBIT
Resp 2
W. Isely 2/4/09

WARNING LETTER
(08-ATL-07)

Dear Mr. Isely:

This is to advise you that the Food and Drug Administration (FDA) has reviewed your websites at the Internet addresses http://www.agaricus.net and http://raaxagaricus.com and has determined that the products "Agaricus dried Grade A," "Agaricus dried Grade A Powder," "Agaricus Capsules," "Agaricus sweet Extract," "Agaricus strong Extract," "RF 1000 Extract," "APM Extract," "RAAX11 Extract," and "OPC Extract" are promoted for conditions that cause the products to be drugs under section 201(g)(1)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 321 (g)(1)(13)]. The therapeutic claims on your websites establish that the products are drugs because they are intended for use in the cure, mitigation, treatment, or prevention of disease. The marketing of these products with these claims violates the Act.

Examples of some of the claims observed on your websites include:

RAAX11 Extract

- "Raax 11 Agaricus Extract ... during laboratory tests the substance destroyed cancer cells that had been resistant to treatment up to now .... '[B]esides these cancer cells, leukemia cells that are normally resistant to a lot of medicines and methods of treatment, were also killed' reported the scientists."

- "Even very resistant Leukemia cells die off"

RAAX11 Extract and OPC Extract

- "The RAAX Agaricus protocol is working at over 99% of all stage IV cancer patients. Even patients with no hope are recovered, if they took the right dosage during the programed [sic] time. What makes the difference between a Chemo Therapy and this kind of treatment. The chemo therapy destroys everything. Using the RAAX agaricus protocol only the cancer cells are destroyed. As effect of this, tumors will shrink very fast."

RF 1000 Extract

- "RF 1000 Extract - Specially used to help at traditional treatments of cancer."

According to your website at http://www.agaricus.net, the products listed in this letter contain Agaricus. Your website lists several disease claims for Agaricus, including:

> •"Cancer - Agaricus blazei Murill ... has an affinity for nourishing the immune system ... there is an inter-dependent relationship between immune status and cancer development."
>
> •"[R]esearchers' findings suggest that the Agaricus water extract reduces the pain associated with breast cancer and may be a viable substitute for the pharmaceuticals that impose side effects. In addition, the researchers noted the anti-tumor effect of the mushroom extract ...." Further, the "Research" page of your website http://www.agaricus.net cites an article about an animal study of the "Agaricus blazei Murill" ingredient used in your products. This article concerns the use of this ingredient for treatment or prevention of cancer.

When scientific publications are used commercially by the seller of a product to promote the product to consumers, such publications may become evidence of the product's intended use. For example, under 21 CFR 101.93(g)(2)(iv)(C), a citation of a publication or reference in the labeling of a product is considered a claim about disease treatment or prevention if the citation refers to a disease use, and if, in the context of the labeling as a whole, the citation implies treatment or prevention of a disease. The citation "Tumor-specific cytocidal and immunopotentiating effects of relatively low molecular weight products derived from the basidiomycete, Agaricus blazei Murill .. Anticancer Res 1999 Jan-Feb;19(IA):113-8" is a reference citation used to market your Agaricus products for disease treatment and prevention on your website.

This reference citation and other claims quoted above are supplemented by the metatags used to bring consumers to your websites through Internet searches. Examples of the metatags include "alternative cancer therapies" and "cancer."

Your products are not generally recognized as safe and effective for the above referenced uses and, therefore, the products are "new drugs" under section 201(p) of the Act [21 U.S.C. § 321(p)]. New drugs may not be legally marketed in the U.S. without prior approval from FDA as described in section 505(a) of the Act [21 U.S.C. § 355(a)]. FDA approves a new drug on the basis of scientific data submitted by a drug sponsor to demonstrate that the drug is safe and effective. Your products "Agaricus dried Grade A," "Agaricus dried Grade A Powder," "Agaricus Capsules," "Agaricus sweet Extract," "Agaricus strong Extract," "RF 1000 Extract," "APM Extract," "RAAX11 Extract," and "OPC Extract" are also misbranded within the meaning of section 502(f)(l) of the Act in that labeling for these drugs fails to bear adequate directions for use [21 U.S.C. § 352(f)(1)].

The above violations are not meant to be an all-inclusive list of deficiencies in your products and their labeling. While reviewing your websites, we noticed that you were also promoting these products for treatment and/or prevention of diseases other than cancer. It is your responsibility to ensure that products marketed by your firm comply with the Act and its implementing regulations. We advise you to review your websites, product labels, and other labeling and promotional materials for your products to ensure that the claims you make for your products do not cause them to violate the Act.

You should take prompt action to correct the violations described above and prevent their future recurrence. Failure to do so may result in enforcement action without further notice. The Act authorizes the seizure of illegal products and injunctions against manufacturers and distributors of those products [21 U.S.C. §§ 332 and 334].

Please notify this office, in writing, within fifteen (15) working days of the receipt of this letter, as to the specific steps you have taken to correct the violations noted above and to assure that similar violations do not occur. Include any documentation necessary to show that correction has been achieved. If corrective actions cannot be completed within fifteen working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be directed to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead. If you wish to discuss this letter, you should contact Mr. Campbell at (404) 253-1280.

Sincerely,

/S/

Mary H. Woleske, Director
Atlanta District

Bolton, Barbara E.

From: Cancer@ftc.gov
Sent: Friday, December 14, 2007 10:30 AM
To: Bolton, Barbara E.
Subject: FW: Urgent Message from the Federal Trade Commission Regarding Cancer Product Advertising on Your Website

-----Original Message-----
From: Cancer@ftc.gov
Sent: Tuesday, October 23, 2007 3:28 PM
To: 'support@ashnow.com'
Subject: Urgent Message from the Federal Trade Commission Regarding Cancer Product Advertising on Your Website

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

TO: www.agaricus.net — Never received

FROM: Federal Trade Commission

RE: Health Claims on Your Website for Cancer Cures and Treatment Products

DATE: October 23, 2007

Deceptive Advertising Claims are Illegal

The staff of the Federal Trade Commission (FTC) recently reviewed your website. We are sending you this letter to remind you of your obligations under the law. The FTC protects consumers from unfair or deceptive advertising or marketing practices that raise health or safety concerns.

The FTC Act prohibits deceptive advertising in any medium, including the Internet. Under the FTC Act, advertising claims for products and services must be truthful and not misleading. Health-related claims, like those made about cancer on your website, must be supported by competent and reliable scientific evidence – the kind of evidence scientists who are experts in the field would rely on. It is against the law to make health claims without scientific support, to exaggerate the benefits of products or services, or to misstate the level of scientific support you have for your claims. Please note that consumer testimonials are not proof that your product works. If you make a health claim through a consumer testimonial, you must have competent and reliable scientific evidence that your product will have the same benefit for other users.

If your website makes express claims (literally made in the ad) or claims by implication (made indirectly or by inference) about the benefits of any cancer-related products or services that are not substantiated by competent and reliable scientific evidence, or are otherwise deceptive or fraudulent, you must stop making those

claims immediately.

http://www.ftc.gov/opa/2001/06/cureall.htmhttp://www.ftc.gov/opa/2001/07/chrisenter.htmhttp://www.ftc.gov.opa/2001/07/chrisenter.htmhttp://www.ftc.gov/opa/2001/07/westbot.htm If ***your website contains any untruthful or unsubstantiated claims, you could face law enforcement action. That could mean:***

1. ***A federal court injunction. Violations of court orders could result in civil penalties or criminal prosecution.***
2. ***An order to pay consumer refunds.***
3. ***Administrative orders with fines up to $11,000 per violation.***

Action Requested

We urge you to review all cancer-related claims on your website. If you don't have competent and reliable scientific evidence to support the claims, please change them immediately or remove them altogether.

FTC investigators have saved your website and will be revisiting it soon. ***Within 10 business days, please send an email to cancer@ftc.gov*** describing the actions you've taken or plan to take to address these concerns.

To ensure that your website complies with the FTC Act, we suggest reviewing the following guidance from the FTC:

1) ***Dietary Supplements: An Advertising Guide for Industry***
www.ftc.gov/bcp/conline/pubs/buspubs/dietsupp.htm
http://www.ftc.gov/bcp/conline/pubs/buspubs/dietsupp.htm/

2. ***Frequently Asked Advertising Questions: A Guide for Small Business***
www.ftc.gov/bcp/conline/pubs/buspubs/ad-faqs.htm

3. ***Advertising and Marketing on the Internet: The Rules of the Road*** at
www.ftc.gov/bcp/conline/pubs/buspubs/ruleroad.htm

Please remember that you are responsible for complying with laws enforced by the Food and Drug Administration (FDA) in addition to laws enforced by the FTC. The Federal Food, Drug, and Cosmetic Act (FDCA) defines a drug, in part, as an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease, or to affect the structure or any function of the body.[1] Drugs that are not generally recognized by qualified, scientific experts as safe and effective for the uses recommended or suggested in their labeling are considered to be new drugs.[2] It is illegal to market a new drug in the U.S. without obtaining prior FDA approval.[3] Violations of the FDCA may result in seizure of illegal products and an injunction against the manufacturers and distributors. We have contacted the FDA about claims on your website. Remember, too,

that unfair or deceptive acts or practices also are illegal under many state laws. The standards under those laws may be different from the FTC Act.

If you are not located in the United States, we have referred the claims on your website to the consumer protection enforcement agency that has jurisdiction in your locale.

We look forward to hearing from you.

1 21 U.S.C. § 321(g).

2 21 U.S.C. § 321(p).

3 21 U.S.C. §§ 355 and 331(d).

United States Patent and Trademark Office

Trademarks > Trademark Electronic Search System (TESS)

TESS was last updated on Wed Apr 9 04:10:56 EDT 2008

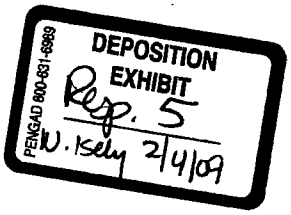
Logout Please logout when you are done to release system resources allocated for you.

Record 1 out of 1

Word Mark	**RAAX11**
Goods and Services	IC 001. US 001 005 006 010 026 046. G & S: Plant extracts, namely ingredients Agaricus blazei Murill and Chrysobalanus Icaco, used in the manufacture of Takesun do Brasil
Mark Drawing Code	(3) DESIGN PLUS WORDS, LETTERS, AND/OR NUMBERS
Design Search Code	26.11.21 - Rectangles that are completely or partially shaded
Serial Number	77337958
Filing Date	November 27, 2007
Current Filing Basis	1B
Original Filing Basis	1B
Owner	(APPLICANT) Takesun Portugal Lda CORPORATION FED REP GERMANY In den Herrenbenden 6 53879 Euskirchen FED REP GERMANY
Description of Mark	The color(s) Red letters on yellow background is/are claimed as a feature of the mark. The mark consists of Red Letters on a yellow background.
Type of Mark	TRADEMARK
Register	PRINCIPAL
Live/Dead Indicator	LIVE

T0000

00000



From: service@paypal.com (service@paypal.com)
To: Riece Miles
Date: Thursday, January 3, 2008 1:08:19 PM
Subject: Receipt for Your Payment to gotto@takesun.com

PayPal *The way to send and receive money online*

Dear Riece Miles,

This email confirms that you have paid (gotto@takesun.com) $134.90 USD using PayPal.

This credit card transaction will appear on your bill as "PAYPAL".

Payment Details

Transaction ID:	20U8900657657914S
Item Price:	$134.90 USD
Total:	$134.90 USD
Order Description:	11263984: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90
Item/Product Number:	11263984
Invoice ID:	11263984
Buyer:	Riece Miles

It may take a few moments for this transaction to appear in the Recent Activity list on your Account Overview.

Business Information

Business:

Your Confirmed Address

Shipping Info: ~~Riece Miles~~ redacted
~~Lorton, VA 22079~~
United States

If you have questions about the shipping and tracking of your purchased item or service, please contact at gotto@takesun.com.

If your email program has problems with hypertext links, then you may also confirm your email address by logging into your PayPal account at www.paypal.com/us. On your My Account page you will find a "Confirm Your Email Address" link. Click on this link and enter the following confirmation

number:

0653-8336-0122-8007-4430

Thank you for using PayPal
The PayPal Team

Your monthly account statement is available anytime; just log in to your account at https://www.paypal.com/us/HISTORY. To correct any errors, please contact us through our Help Center at https://www.paypal.com/us/HELP.

FOR INTERNATIONAL PAYMENTS ONLY

Commissions and Fees incurred by sender: $0.00

Rate of Exchange: The above exchange rate includes a 2.5% spread above the wholesale exchange rate at which PayPal obtains foreign currency, and the spread is retained by PayPal. If and when the Recipient chooses to withdraw these funds from the PayPal System, and if the withdrawal involves a currency conversion, the Recipient will convert the funds at the applicable currency exchange rate at the time of the withdrawal, and the Recipient may incur a withdrawal fee.

RIGHT TO REFUND
You, the customer, are entitled to a refund of the money to be transmitted as a result of this agreement if PayPal does not forward the money received from you within 10 days of the date of its receipt, or does not give instructions committing an equivalent amount of money to the person designated by you within 10 days of the date of the receipt of the funds from you unless otherwise instructed by you.

If your instructions as to when the money shall be forwarded or transmitted are not complied with, and the money has not yet been forwarded or transmitted, you have a right to a refund of your money.

If you want a refund, you must mail or deliver your written request to PayPal at P.O. Box 45950, Omaha, NE 68145-0950. If you do not receive your refund, you may be entitled to your money back plus a penalty of up to $1,000.00 USD and attorney's fees pursuant to Section 1810.5 of the California Financial Code.

Important Note: The Right to Refund claim process applies only to payments that have not been successfully transmitted to the recipient. With PayPal, almost all payments are transmitted to the recipient immediately, except for eCheck payments, and payments to non-PayPal members.

Please do not file a Right to Refund claim if your payment has already been completed. If you have problems with a completed payment or need assistance with settling a dispute with a seller, go to PayPal's Resolution Center by logging into your account and clicking the Resolution Center sub tab located at the top center of the Account Overview page.

You can also click the Help link at the top right of any PayPal page to look up more information about the Resolution Center and filing complaints.

MA residents only: PayPal holds a Foreign Transmittal Agency license in the State of Massachusetts - License Number FT3345.

Please do not reply to this email. This mailbox is not monitored and you will not receive a response. For assistance, log in to your PayPal account and choose the Help link located in the top right corner of any PayPal page.

To receive email notifications in plain text instead of HTML, update your preferences here.

PayPal Email ID PP120

gotto@takesun.com

Receipt

PayPal Secure Payments

Ship To: Riece Miles
Lorton, VA 22079
United States

redacted

Seller Information: gotto@takesun.com

Transaction ID: 20U8900657657914S

Placed on Jan. 3, 2008

Payment For	Quantity	Price
11263984: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90 Item #11263984	1	$134.90 USD
	Subtotal:	$134.90 USD
	Sales Tax:	$0.00 USD
	Total Amount:	**$134.90 USD**

Print Done

PayPal. The safer, easier way to pay.
For more information, read our User Agreement and Privacy Policy.

citi

Statement Date
01/15/08

INDIVIDUAL CARDHOLDER ACTIVITY

MILES.RIECE -9704

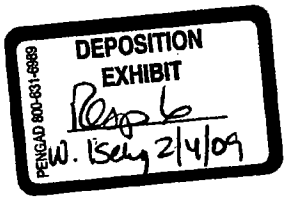
Monthly Limit	Cash Limit*
$3,000	$3,000

Sale Date	Post Date	Reference Number	Type of Activity	Amount
01-03	01-07	24492158004849784728500	PAYPAL 402-935-7733 CA	134.90
			TOTAL PURCHASES/ADVANCES/CREDITS	134.90

*Cash Advance Limit is a portion of your Total Monthly Limit
**Available Cash Line is a portion of your Available Credit Line

Takesun do Brasil

Verifiy that you are in following countries: USA, Canada, Australia or Asia. Other countries will be delivered through other agents. Look into your country page. (EU-Distributors: Austria, Germany, Portugal, Spain)or contact sales@agaricus.net



Product	Quantity	Price	Amount
Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original	1	119.90	119.90

	Subtotal	119.90
All prices are in US Dollars	Shipping	15.00
	TOTAL	134.90

US customers: UPS ground: 5 business days, UPS air: 3 business day delivery. International customers only Asia & Australia. Europe enter in your country page: EMS shipping arrives within 5-10 working days, Global Priority Mail 10 to 18 days.

Billing details

Dana Long
redacted
Roanoke, VA 24018
United States
Tel : 703-532-
Fax :
dana_long@yahoo.com

Shipping address (If different from the billing address)

Payment options

◉ Credit card or direct cash payment via **PayPal**

CONTINUE

Your Credit Card is charged using a SSL secured server. On your statement will apear GEMTRONICS SECURE PAYMENTS

From: service@paypal.com (service@paypal.com)
To: Dana Long
Date: Wednesday, January 23, 2008 11:27:52 AM
Subject: Receipt for Your Payment to Takesun Portugal Lda. Verkauf Deutschland

PayPal *The way to send and receive money online*

Dear Dana Long,

This email confirms that you have paid Takesun Portugal Lda. Verkauf Deutschland (vendas@takesunportugal.com) $134.90 USD using PayPal.

This credit card transaction will appear on your bill as "PAYPAL *TAKESUNPORT".

Payment Details

Transaction ID:	00061355NC651964H
Item Price:	$134.90 USD
Total:	$134.90 USD
Order Description:	11306829: 1 Agaricus blazei murill Raax11 bottle 100ml melhor qualidade original @ 119.90
Item/Product Number:	11306829
Invoice ID:	11306829
Buyer:	Dana Long
Phone:	703-532-

It may take a few moments for this transaction to appear in the Recent Activity list on your Account Overview.

Business Information

Business:	Takesun Portugal Lda. Verkauf Deutschland
Contact E-Mail:	vendas@takesunportugal.com

Your Unconfirmed Address

Shipping Info: Dana Long — redacted
Roanoke, VA 24018
United States

If you have questions about the shipping and tracking of your purchased item or service, please contact Takesun Portugal Lda. Verkauf Deutschland at vendas@takesunportugal.com.

Thank you for using PayPal!
The PayPal Team

Your monthly account statement is available anytime; just log in to your account at https://www.paypal.com/us/HISTORY. To correct any errors, please contact us through our Help Center at https://www.paypal.com/us/HELP.

FOR INTERNATIONAL PAYMENTS ONLY

Commissions and Fees incurred by sender: $0.00

Rate of Exchange: The above exchange rate includes a 2.5% spread above the wholesale exchange rate at which PayPal obtains foreign currency, and the spread is retained by PayPal. If and when the Recipient chooses to withdraw these funds from the PayPal System, and if the withdrawal involves a currency conversion, the Recipient will convert the funds at the applicable currency exchange rate at the time of the withdrawal, and the Recipient may incur a withdrawal fee.

RIGHT TO REFUND
You, the customer, are entitled to a refund of the money to be transmitted as a result of this agreement if PayPal does not forward the money received from you within 10 days of the date of its receipt, or does not give instructions committing an equivalent amount of money to the person designated by you within 10 days of the date of the receipt of the funds from you unless otherwise instructed by you.

If your instructions as to when the money shall be forwarded or transmitted are not complied with, and the money has not yet been forwarded or transmitted, you have a right to a refund of your money.

If you want a refund, you must mail or deliver your written request to PayPal at P.O. Box 45950, Omaha, NE 68145-0950. If you do not receive your refund, you may be entitled to your money back plus a penalty of up to $1,000.00 USD and attorney's fees pursuant to Section 1810.5 of the California Financial Code.

Important Note: The Right to Refund claim process applies only to payments that have not been successfully transmitted to the recipient. With PayPal, almost all payments are transmitted to the recipient immediately, except for eCheck payments, and payments to non-PayPal members.

Please do not file a Right to Refund claim if your payment has already been completed. If you have problems with a completed payment or need assistance with settling a dispute with a seller, go to PayPal's Resolution Center by logging into your account and clicking the Resolution Center sub tab located at the top center of the Account Overview page.

You can also click the Help link at the top right of any PayPal page to look up more information about the Resolution Center and filing complaints.

MA residents only: PayPal holds a Foreign Transmittal Agency license in the State of Massachusetts - License Number FT3345.

Please do not reply to this email. This mailbox is not monitored and you will not receive a response. For assistance, log in to your PayPal account and choose the Help link located in the top right corner of any PayPal page.

To receive email notifications in plain text instead of HTML, update your preferences here.

PayPal Email ID PP120

TAKESUN
Takesun do Brasil Ind. Com e Exp. Ltda.
Av. Vereador Benedito de Campos, 516
Ibiúna, SP, CEP 18150-000, Brasil
Fone xx15 3248 1267 - Fax xx 15 3248 3270
e-mail: vendas@takesun.com
Internet: www.takesun.com

FDA Food Facility Registration Number 11841249604

INVOICE

paid by FDA Registration No. 10827550148 964
Isely, William H. Gemtronics,Naturefirst
aka Nature First

, Walnut Creek, RD, 28734
Franklin, NC, USA
Phone 828 369 7590

Shipping to Danzas Acct # 56-226120600
Isely, William H. Gemtronics,Naturefirst
aka Nature First
FDA Registration No. 10827550148
964, Walnut Creek, RD, 28734
Franklin, NC, USA
Phone 828 369 7590

Numero 306
Data 27th February 2003

PURCHASE ORDER NO. S/N
TERMS Banco do Brasil
SALES PERSON George Otto
SHIPPED VIA Danzas/DHL
INCO Terms ex works
Delivery 27th February 2004

QTY KG	NCM Brasil	US Tariif		Unit USD	Total USD
10	07.12.31.00	0712.31.10 00	Agaricus blazei Murill, dried mushrooms, packed in into 100g bags	10,07	100,70
140	1302.1900	1302.19.90.40	Agaricus bl. Murill, bottle with 60 Vcaps, 500mg	6.00	840.00
72	1302.1900	1302.19.90.40	Agaricus RF 1000 extract, bottle with 200ml	9.89	712.00
144	1302.1900	1302.19.90.40	Agaricus ABM extract, bottle with 100ml	9.90	1425.60
240	2008.9900	2008.99.6000	Myrciarai dubia, Camu-Camu, bottle with 60 capsules	**4.15**	996.00

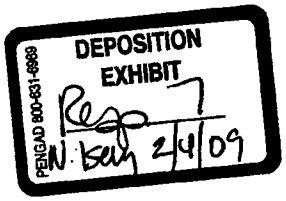
FDA Product

Code: 1) 54FBK99 2) 54FBK99

Merchandise	4074.30
Insurance	0.00%
	0.00
Freight	0.00
	4,074.30
	TOTAL DUE

Takesun do Brasil USA FDA Agents: Gomez & FDA Associates FDA Experts, 3509 W. Beverly Blvd. ,Montebello, CA, 90640,USA, Tel. 323-707-2504, e-mail: irenegomez@fdaexperts.com

Boxes total:	8
Liq. Weight total:	78,2 kg
Brut Weight total:	84,6kg
Cubic weight:	55,5 kg
Dimensiones Boxes cm:	38x42x42
Signed:	
Name:	
CPF:	



00034

DomainDiscover
DOMAIN REGISTRATION SERVICES

To whom it may concern,

I hereby confirm that the information listed for the domain **agaricus.net** is legitimate and is listed below:

Registrant:
Agarix International
Br 101, KM 22,5
Joinville, SC 89239500
Brazil
47 3001 5260
gotto@takesun.com.br

Domain Name: AGARICUS.NET

Administrative Contact, Technical Contact, Zone Contact:
Takesun
Attn: George Otto
Br 101, KM 22,5
Joinville, SC 89239500
Brazil
47 3001 5260
gotto@takesun.com.br

Domain created on 13-Jun-1998
Domain expires on 12-Jun-2009
Last updated on 15-Apr-2008

Domain servers in listed order:

DNS1.SUPREMEDNS.COM
DNS2.SUPREMEDNS.COM

Sincerely,
Pablo Velasco
TierraNet Customer Service Supervisor

PENGAD 800-631-6989
DEPOSITION EXHIBIT
Resp 8
W. Isely 2/4/09

COMPLAINT COUNSEL'S EXHIBIT 4

REPORT OF OMER KUCUK, M.D.

I. Education, Experience And Training

1. I am a Doctor of Medicine, and obtained my medical degree from Hacettepe University Medical School, Ankara, Turkey in 1975. My post-graduate training included Medical Internship and Residency, St. Francis Hospital, Evanston, Illinois (1975 - 1978); Hematology-Oncology Fellowship, St. Francis Hospital, Evanston, Illinois (1978 - 1979); and Hematology-Oncology Fellowship, Northwestern University Medical School, Chicago, Illinois (1979 - 1981). I have been a practicing in the field of hematology and medical oncology for over 27 years, and my areas of expertise include cancer prevention, nutrition and cancer, chemoprevention, chemotherapy, medical oncology and clinical trials. I also specialize in translational research focusing on the therapeutic effects of botanical compounds on cancer patients. I am Board Certified with the American Board of Internal Medicine, Subspecialty of Hematology, and Subspecialty of Medical Oncology. My curriculum vitae is attached hereto as **Exhibit A**.

2. Currently, I am Acting Professor of Hematology and Medical Oncology, Department of Hematology and Medical Oncology, Emory University School of Medicine, Winship Cancer Institute, in Atlanta, Georgia. I am also attending physician at the Emory University Hospital, the Emory Crawford Long Hospital, and the Grady Hospital in Atlanta, Georgia. As Chief of Genitourinary Medical Oncology at the Department of Hematology and Oncology, I lead a group of medical oncologists and clinical researchers treating cancers of the prostate, bladder, kidney and testis and conduct clinical research related to these cancers. I also lead the Prostate Cancer Translational Research Group at Emory University, which conducts collaborative translational research projects in prostate cancer.

3. I have engaged in scholarly research and writing relating to cancer and the treatment of cancer for over 27 years. I have authored or co-authored approximately 125 articles published in peer-reviewed scientific journals and more than 20 published book chapters and reviews. A majority of these pertain to cancer and/or cancer-relate conditions. Several of the peer-review articles that I have authored or co-authored reported on the results of randomized, double-blind, placebo-controlled clinical studies examining the efficacy of botanical compounds.

4. My research focuses on the use of clinical trials in appropriate populations to demonstrate the efficacy and mechanisms of cancer preventive compounds in humans. Biomarkers of cancer risk and progression are used as intermediate endpoints and their modulation by chemopreventive agents are demonstrated in small clinical studies prior to the initiation of larger Phase III clinical trials. Current investigations focus on the effects of micronutrients and phytochemicals on biomarkers of cell proliferation, differentiation, apoptosis and oxidative stress in a variety of cancers. I also investigate the modulation of genetic and epigenetic pathways of carcinogenesis by nutritional interventions. A major focus of my research is bringing botanical compounds from the laboratory to the clinic by conducting translational research studies. I have conducted the first clinical trials with tomato lycopene and soy isoflavones in prostate and breast cancer patients.

5. I currently am on the Editorial Boards of the peer-reviewed publications *Annals of Medical Sciences, Cancer Epidemiology, Biomarkers and Prevention, Turkish Journal of Cancer, International Journal of Hematology and Oncology,* and *Advances in Molecular Medicine.* I am a Guest Editor of *Cancer and Metastasis Reviews* and an Assistant Editor of *Cancer Detection and Prevention.* I have participated in the peer review of hundreds of papers submitted for publication to cancer-related scientific journals, many of which concerned randomized, double-blinded, placebo-controlled studies. In reviewing these submissions, I evaluate, among other things, the adequacy of the design and conduct of the clinical research and the adequacy and accuracy of the statistical analysis.

6. I keep current on new developments and research in the treatment of cancer through memberships in professional societies including the American Society of Clinical Oncology, American Association for Cancer Research, American Society of Preventive Oncology, American Society for Nutrition, American College of Nutrition (Fellow), American Urological Association, Society for Free Radical Biology and Medicine, American Head and Neck Society, and Society of Basic Urological Research. I also have had the following memberships: Member, Scientific Advisory Board, Fifth International Symposium on the Role of Soy in Preventing and Treating Chronic Disease (2003); and Member, Scientific Advisory Board, Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease (1999).

7. In addition, I have held committee memberships on national and international panels and committees including Member of Scientific Committee, International Meeting "Molecular Targets for Cancer Prevention, Diagnosis, and Treatment" (2007); Member: US Department of Veterans Affairs Medical Research Service Merit Review Subcommittee for Oncology (2001-2004); Member: NCI Special Emphasis Panel, Molecular Targets for Nutrients in Prostate Cancer Prevention (2002); Member: Site Visit Team, NIH Cancer Center Support Grant, University of California Irvine Cancer Center (2002); Member: NCI Special Emphasis Panel, Innovative Cancer Complementary and Alternative Medicine Initiative in Cancer Centers (2001); Member: NCI Special Emphasis Panel for Small Grants in Cancer Chemoprevention (2000); Member: NCI Special Emphasis Panel, Phase II Chemoprevention Master Agreement Applications (1999); Member: NCI Special Emphasis Panel, Tobacco Use Research Center (P50) Applications (1999); Member: NCI Special Emphasis Panel, Phase I and Phase II Clinical Studies of Chemopreventive Agents (1999); Member of AACR Program Committee, AACR Clinical Prevention Studies Section, Prevention Subcommittee (1998); and Member: NCI Special Emphasis Panel, Program Project Applications for Chemoprevention Studies in High-risk Populations (1997).

8. Honors that I have received in connection with my work in cancer research and education include: Best Doctors in America® (2007-2008, 2005-2006, 2003-2004, 2001-2002); America's Top Physicians (2006); College Teaching Award, Wayne State University (2006, 2002); Faculty Research Excellence Award, School of Medicine, Wayne State University (2000); President's Achievement Award for Outstanding Service, Karmanos Cancer Institute (2000); and College Teaching Award, Wayne State University (1998).

9. Based upon my knowledge, experience and training, I consider myself to be qualified as

an expert in the fields of cancer research and treatment. As a result of my own research and my ongoing editorial duties for peer-reviewed scientific publications, I also consider myself to be qualified as an expert in evaluating the design and execution of clinical studies in the area of cancer research.

10. During the preceding four years, I have provided expert testimony in the following legal proceeding: Minnesota Board of Medicine v. Fatih Uckun. I am being compensated at the rate of $400 per hour for my work in this litigation.

II. Scope of the Report and Conclusions

11. The FTC staff has requested that I evaluate, from my perspective as an expert in the research and treatment of cancer, whether the following claims for the product RAAX11 are supported:

A) Reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer;

B) RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel; and

C) RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer.

12. To accomplish this task, I have reviewed the RAAX11 product label, which states:

Takesun® RAAX11, Strong Water Extract, A Dietary Supplement, Net 100 ml.

Supplement Facts
Serving Size 2.5 ml.
Servings per container: 40
Amount Per Serving
Proprietary Blend - 2.5 ml.*
Chrysobalanus Icaco extract
Agaricus blazei Murill mushroom extract
* Daily values not established
Other Ingredients: Distilled Water
FDA Product Code: 54FB99

The suggested use is 2.5 ml. in tea or water, one to three times a day. Although the product label states that the bottle contains 100 ml., there is no indication of how much of either ingredient is contained in the product.

13. I conducted an independent search of studies published in English language journals to

determine whether there are studies that provide scientific support for the claims made for RAAX11 and the combination of *icaco* and *agaricus* that comprises the formulation of RAAX11.

14. I also have reviewed each of the documents identified in **Exhibit B** to this declaration, which materials I am informed were provided to the FTC by the respondents in this action.

15. In brief, the studies I have reviewed do not provide reliable scientific support for any of the challenged claims for RAAX11. With respect to the claim that reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer, it must be stated up-front that cancer is not a single disease but many different diseases. The existing body of scientific evidence does not provide competent and reliable evidence that RAAX11, or either of its ingredients *icaco* or *agaricus*, alone or in combination, has been proven to or effectively can prevent, treat or cure any form of cancer.

A. Scientific Research on RAAX11

16. To my knowledge, and based on my search of the scientific literature, there is no published scientific literature evaluating the efficacy of RAAX11. There are no Phase I or II clinical trial data with RAAX11. Accordingly, there is no basis for the claims that A) reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer; B) RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel; and C) RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer.

17. Further, the formulation that comprises RAAX11 is a combination of the two extracts which may interact with each other and there is again no published scientific literature (human, animal, or laboratory) evaluating the combination of *icaco* and *agaricus.* A search of the scientific literature revealed no article about the efficacy of taking the combination of *icaco* and *agaricus* as a cancer treatment, or even looking at potential mechanisms of anticancer activity. The scientific literature concerning *icaco* and *agaricus* is limited and insufficient to adequately support therapeutic claims that RAAX11 is effective for the prevention, treatment, and cure of cancer.

(1) *Chrysobalanus icaco*

18. I am not aware of any competent and reliable scientific evidence indicating that *Chrysobalanus icaco,* which is from a tropical bush,[1] has therapeutic benefits in humans. My search of the scientific literature revealed only four publications with *Chrysobalanus icaco.* None of these reports were on animal or human studies. Rather, they only reported the results of

[1] The RAAX11 package label does not indicate whether the extract is made from the bark, leaf, root, or other part of the *icaco* plant.

in vitro studies. The evidence regarding *Chrysobalanus icaco* is therefore considered rudimentary and no inferences can be made on the usefulness of *Chrysobalanus icaco* in humans. There are no animal or human data published in reputable peer-reviewed scientific journals showing its efficacy, toxicity, and appropriate dosing. Before any recommendations can be made regarding the use of *Chrysobalanus icaco* in humans, research including at least Phase I and Phase II clinical trials are needed. Thus, the existing body of scientific evidence does not provide competent and reliable evidence that *Chrysobalanus icaco*, alone or in combination with *agaricus*, has been proven to or effectively can prevent, treat or cure any form of cancer.

19. The four publications regarding *Chrysobalanus icaco* that I examined were:

1) De Brito, ES *et al.* Anthocyanins present in selected tropical fruits: acerola, jambolão, jussara, and guajiru. J Agric Food Chem. 2007;55(23):9389-94.

2) Ferreira-Machado, SC *et al.* Genotoxic potentiality of aqueous extract prepared from Chrysobalanus icaco L. leaves. Toxicol Lett. 2004;151(3):481-7.

3) Fernandes, J *et al.* Pentacyclic triterpenes from Chrysobalanaceae species: cytotoxicity on multidrug resistant and sensitive leukemia cell lines. Cancer Lett. 2003;190(2):165-9.

4) Alves De Paulo, S *et al.* Chrysobalanus icaco L. extract for antiangiogenic potential observation. Int J Mol Med. 2000;5(6):667-9.

(2) *Agaricus blazei murill*

20. My search of the scientific literature revealed 107 articles regarding *Agaricus blazei.* However, there are only eight publications reporting the results of clinical or human studies with *Agaricus blazei*. There are no reports of properly conducted Phase I and Phase II clinical trials regarding the toxicity and efficacy of *Agaricus blazei* extract in patients with cancer. Therefore, no conclusions can be made with regard to the efficacy or toxicity of the extract in cancer patients. No recommendations can be made regarding the safe and efficacious dose of the extract. Here too, the existing body of scientific evidence does not provide competent and reliable evidence that *Agaricus blazei*, alone or in combination with *icaco*, has been proven to or effectively can prevent, treat or cure any form of cancer.

21. My summary of the eight clinical publications on *Agaricus blazei* is as follows:

1) Liu, Y *et al.* Immunomodulating Activity of Agaricus brasiliensis KA21 in Mice and in Human Volunteers. Evidence based Complement Alt Med 2008;5(2):205-219.

Liu *et al.* had clinical research performed on 31 healthy subjects who were not taking any medication prior to or at the time of the study. The subjects were divided into three groups, group 2 and group 3 (total 20 subjects) were administered the normal dose, and group 1 (11

subjects) were administered a 3-fold higher dose (safety clinical study group) of *A. brasiliensis*.

Group 1. For 6 months, the 11 subjects (mean age 43.6 ± 12.6 years, male 6, female 5) were asked to take 30 tablets/day (divided into three administrations; each tablet contained 300 mg of *A. brasiliensis*), which is three times the normal dose. Then, the study measured and analyzed subjective changes in their condition, liver function (GOT, GPT, γ-GTP), renal function [blood urea nitrogen (BUN), creatinine] and nutritional status (total protein).

Group 2. For 3 months, 12 subjects (mean age 45.3 ± 8.1 years, male 9, female 3) were asked to take the normal dose of 10 tablets/day (divided into two administrations; each tablet contained 300 mg of *A. brasiliensis*). Then, the study measured body weight, BMI, percentage body fat, percentage visceral fat and blood biochemical levels (total protein, blood glucose, cholesterol, neutral fat, GOT, GPT and γ-GTP).

Group 3. For 3 months, 8 subjects (mean age 22.3 ± 0.5 years, male 6, female 2) were asked to take the normal dose, and immune function (NK cell count, NK cell activity) was measured. In the measurement of immune function, the study divided the eight subjects into two groups in a double-blind manner, *A. brasiliensis* group and placebo group, administered 10 tablets/day (divided into two administrations; each tablet contained 300 mg of *A. brasiliensis*) for 7 days, and determined NK cell count and NK cell activity in peripheral blood. After two-month drug withdrawal, the same study was conducted with the tablets exchanged (crossover).

Taken together, the study determined that both lipid and blood glucose levels showed a decreasing trend for lifestyle-related diseases. In addition, an improvement in liver function was noted.

2) Hsu C-H *et al.* The Mushroom Agaricus blazei Murill Extract Normalizes Liver Function in Patients with Chronic Hepatitis B. J Alt Complement Med 2008, 14(3): 299-301.

Hsu *et al.* (2008) reported on four (4) patients with hepatitis B who met the criteria (1) aged between 20 and 65 years; (2) being Chinese; (3) having been a hepatitis B carrier (HBAg(+)) for more than 3 years; (4) alanine aminotransferase > 100 IU/L; and (5) not taking lamivudine, α-interferon, or other drugs for hepatitis participated in the study. The enrolled patients were given *Agaricus blazei* Murill (ABM) extract of 1500 mg daily for 12 months. At the end of the study, the mean level of aspartate aminotransferase and alanine aminotransferase decreased from 246.0 (± standard deviation [SD] 138.9) to 61.3 (± SD 32.6) IU/L and 151.0 (± SD 86.9) to 46.1 (± SD 22.5) IU/L, respectively. The study concluded that their initial observation seemed to indicate the potential benefit of ABM extract in normalizing liver function of patients with hepatitis B.

3) Talcott, JA *et al.* Measuring perceived effects of drinking an extract of basidiomycetes Agaricus blazei Murill: a survey of Japanese consumers with cancer. BMC Complement Altern Med. 2007; 7:32.

Talcott *et al.* (2007) designed, translated and mailed a survey to 2,346 Japanese consumers of Sen-Sei-Ro (extract of the Basidiomycetes *Agaricus blazei* Murill mushroom) self-designated as cancer patients. The survey assessed consumer demographics, cancer history, Sen-Sei-Ro consumption, and its perceived effects. They received completed questionnaires from 782 (33%) of the sampled Sen-Sei-Ro consumers with a cancer history. The survey respondents represented a broad range of cancer patients familiar with Sen-Sei-Ro. Nearly all had begun consumption after their cancer diagnosis. These consumers expressed consistently positive views, though not extremely so, with more benefit reported for more abstract benefits such as emotional and physical well-being than relief of specific symptoms.

4) Hsu, CH *et al.* The mushroom Agaricus Blazei Murill in combination with metformin and gliclazide improves insulin resistance in type 2 diabetes: a randomized, double-blinded, and placebo-controlled clinical trial. J Altern Complement Med. 2007;13(1):97-102.

Hsu *et al.* (2007) conducted a study which was a clinical randomized, double-blind, placebo-controlled trial of a population of 536 registered diabetes patients with 72 subjects (1) aged between 20 and 75 years, (2) being Chinese, (3) having type 2 diabetes for more than 1 year, and (4) having been taking gliclazide and metformin for more than 6 months were enrolled in this study. The enrolled patients were randomly assigned to either receiving supplement of *Agaricus blazei* Murill (ABM) extract or placebo (cellulose) 1500 mg daily for 12 weeks. At the end of the study, subjects who received supplement of ABM extract ($n = 29$) showed significantly lower HOMA-IR index (3.6[standard deviation, 2.5] versus 6.6[standard deviation, 7.4], $p = 0.04$) than the control group ($n = 31$). The plasma adiponectin concentration increased 20.0(standard deviation, 40.7)% in the ABM group after 12 weeks of treatment, but decreased 12.0(20.0)% among those taking the placebo ($p < 0.001$). They concluded that the supplement of ABM extract improved insulin resistance among subjects with type 2 diabetes. The increase in adiponectin concentration after taking ABM extract for 12 weeks might be the mechanism that brings the beneficial effect.

5) Mukai, H *et al.* An alternative medicine, Agaricus blazei, may have induced severe hepatic dysfunction in cancer patients. Jpn J Clin Oncol. 2006; 36(12):808-10.

Mukai *et al.* (2006) reported three (3) cases of patients with advanced cancer who showed severe hepatic damage, and two of whom died of fulminant hepatitis after taking *Agaricus blazei* (Himematsutake) extract, one of the most popular complementary and alternative medicines among Japanese cancer patients. In one patient, liver functions recovered gradually after she stopped taking the *Agaricus blazei*, but she restarted taking it, which resulted in deterioration of the liver function again. The other patients who were admitted for severe liver damage had started taking the *Agaricus blazei* several days before admission. Although several other factors could not be completely ruled out as the causes of liver damage, a strong causal relationship between the *Agaricus blazei* extract and liver damage was suggested.

6) Grinde, B *et al.* Effects on gene expression and viral load of a medicinal extract

from Agaricus blazei in patients with chronic hepatitis C infection. Int Immunopharmacol. 2006; 6(8):1311-4.

Grinde *et al.* (2006) reported the effect *Agaricus blazei* Murrill (AbM) on gene expression in peripheral blood cells from four (4) chronic hepatitis C patients, using global (29 k) oligo-based, single channel microarrays. The viral load was slightly, but not significantly, decreased after 1 week of AbM treatment. The more notable changes in mRNA levels were related to genes involved in the G-protein coupled receptor signaling pathway, in cell cycling, and in transcriptional regulation.

7) Yoshimura K, *et al.* Use of complementary and alternative medicine by patients with urologic cancer: a prospective study at a single Japanese institution. Support Care Cancer. 2005; 13(9):685-90.

Yoshimura *et al.* (2005) studied 349 patients with newly diagnosed urologic cancer who answered a self-administered questionnaire on Complementary and Alternative Medicine (CAM) use one year after diagnosis. General-health-related quality of life (GHQL) of the patients was also assessed at diagnosis and one year after diagnosis using the Medical Outcome Study Short Form-36 (SF-36). 164 respondents (47%) admitted using some type of CAM, of which 73 (45%) had used multiple types. "Health food," in particular, extract from *Agaricus blazei*, was the most common type of CAM used. CAM users had significantly lower scores for social function, general health perception, and vitality domains than CAM non-users one year after diagnosis. This tendency was more marked in users of multiple types of CAM.

8) Ahn, WS *et al.* Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, Agaricus blazei Murill Kyowa, in gynecological cancer patients undergoing chemotherapy. Int J Gynecol Cancer. 2004; 14(4):589-94.

Ahn *et al.* (2004) investigated the effects of *Agaricus blazei* Murill Kyowa (ABMK) consumption on immunological status and qualities of life in cancer patients undergoing chemotherapy. One hundred (100) cervical, ovarian, and endometrial cancer patients were treated either with carboplatin plus etoposide, or with carboplatin plus taxol every 3 weeks for at least three cycles with or without oral consumption of ABMK. The natural killer cell activity was significantly higher in ABMK-treated group (ANOVA, $n = 39$, $P < 0.002$) as compared with nontreated placebo group ($n = 61$). Chemotherapy-associated side effects such as appetite loss, alopecia, emotional instability, and general weakness were improved by ABMK treatment. Taken together, this suggests that ABMK treatment might be beneficial for gynecological cancer patients undergoing chemotherapy.

22. While there is some research concerning treatment of cancer with medicinal mushrooms, more research is needed before it will be possible to determine whether this might be an effective cancer treatment in humans. Medicinal mushrooms contain beta-glucan, a substance that seems to activate natural killer cells in the immune system, which can be cytotoxic (toxic to cells). However, these laboratory studies also show no effect in curing cancer. Additional

laboratory studies are investigating other potential anticancer mechanisms of action, but this research, too, is preliminary and insufficient to support any therapeutic claims for medicinal mushrooms.

III. Brief Overview of Cancer

23. The term "cancer" is used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems. Cancer is not just one disease but many diseases. There are more than 100 different types of cancer. Most cancers are named for the organ or type of cell in which they start. For example, cancer that begins in the colon is called colon cancer; cancer that begins in basal cells of the skin is called basal cell carcinoma.

24. Cancer types can be grouped into broader categories. The main categories of cancer include Carcinoma (cancer that begins in the skin or in tissues that line or cover internal organs); Sarcoma (cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue); Leukemia (cancer that starts in blood-forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and enter the blood); Lymphoma and myeloma (cancers that begin in the cells of the immune system); and Central nervous system cancers (cancers that begin in the tissues of the brain and spinal cord).

25. All cancers begin in cells. The body is made up of many types of cells. These cells grow and divide in a controlled way to produce more cells as they are needed to keep the body healthy. When cells become old or damaged, they die and are replaced with new cells. However, sometimes this orderly process goes wrong. The genetic material or DNA of a cell can become damaged or changed, producing mutations that affect normal cell growth and division. When this happens, cells do not die when they should and new cells form when the body does not need them. The extra cells may form a mass of tissue called a tumor.

26. Not all tumors are cancerous: tumors can be benign or malignant. Benign tumors are not cancerous. They can often be removed, and, in most cases, they do not come back. Cells in benign tumors do not spread to other parts of the body. Malignant tumors are cancerous. Cells in these tumors can invade nearby tissues and spread to other parts of the body. The spread of cancer from one part of the body to another is called metastasis. Some cancers do not form tumors. For example, leukemia is a cancer of the bone marrow and blood.

27. Cancer is caused by changes in genes that normally control the growth and death of cells. Certain lifestyle and environmental factors can change some normal genes into genes that allow the growth of cancer. Many gene changes that lead to cancer are the result of tobacco use, diet, exposure to ultraviolet (UV) radiation from the sun, or exposure to carcinogens (cancer-causing substances) in the workplace or in the environment. Some gene alterations are inherited from one or both parents. However, having an inherited gene alteration does not always mean that the person will develop cancer; it only means that the chance of getting cancer is increased. Scientists continue to examine the factors that may increase or decrease a person's chance of developing cancer. Being infected with certain viruses, such as the human papillomavirus

(HPV), hepatitis B and C, and human immunodeficiency virus (HIV), can increase the risk of some types of cancer.

28. Cancer can be treated by wide range of therapies and treatments such as chemotherapy, radiation, surgery, hyperthermia (treating tumors with heat), angiogenesis inhibition (cutting off blood supply to the tumor); biological therapies; and bone marrow transplantation, to name a few. These treatments are administered by experts trained as surgical oncologists, radiation oncologists, medical oncologists, hematologic oncologists or pediatric oncologists depending on the type of treatment used and the age group of the patient.

29. Many cancers are curable if they are diagnosed and treated at an early stage. Most cancers are incurable when they are detected at a later stage. Generally, solid tumors are classified as stage I to IV. The higher the stage, the more advanced is the disease. The stage number is determined by the size of the tumor, invasion of local tissues, and metastases to the lymph nodes and distant organs. Further, the higher the stage, the more difficult the cancer is to cure. Early stage cancers are amenable to surgical resection or radiation therapy which is frequently curative. However, late stage tumors, that have spread beyond the initial site of the tumor, are generally incurable and are treated with a combination of therapies which usually include chemotherapy.

30. There is no guaranteed way to prevent cancer. However, individuals can reduce their risk of developing cancer by: not using tobacco products; choosing foods with less fat and eating more vegetables, fruits, and whole grains; exercising regularly and maintaining a lean weight; avoiding the harmful rays of the sun, using sunscreen, wearing clothing that protects the skin; and talking with a doctor about the possible benefits of drugs proven to reduce the risk of certain cancers. Although many risk factors can be avoided, some, such as inherited conditions, are unavoidable. Not everyone with a particular risk factor for cancer, however, actually gets the disease. Individuals who have an increased likelihood of developing cancer can help protect themselves by avoiding risk factors whenever possible and by getting regular checkups so that, if cancer develops, it is likely to be found and treated early. As stated above, treatment is often more effective when cancer is detected early. Cancer prevention studies to explore ways to reduce the risk of developing cancer are evaluating dietary supplements, chemopreventive agents, nutrition, personal behaviors, and other factors that may prevent cancer.

31. It is estimated that approximately 1.4 million Americans will develop cancer this year and approximately 600,000 Americans will die of the disease. The largest numbers of cancer cases recorded are the cancers of prostate, breast, colon and lung. These cancers are not curable regardless of the type of treatment used when they are at an advanced stage.

IV. General Requirements For Reliable Scientific Support For The RAAX11 Claims

32. As noted previously, cancer is not a single disease but many different diseases, and there is no known treatment that is generally accepted as effective for all forms of cancer. Cancer treatment claims must be supported by randomized, well-controlled, and double-blinded clinical trials demonstrating the product's efficacy for the specific type(s) of cancer for which the claims

are made.

33. The FTC staff has asked me what kind of evidence experts in the field of cancer research and treatment would require to support each of the following claims challenged for the RAAX11 product:

A) Reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer;

B) RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel; and

C) RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer.

34. In my opinion, qualified experts in the field of oncology would require that all such claims be supported by well-conducted, placebo-controlled, randomized, double-blind, clinical trials involving a sufficiently large population from which data on the appropriate endpoint(s) are collected at meaningful intervals over an appropriate period of time. Preferably, such clinical trials should be "multi-center" trials conducted on like groups of subjects at several research centers. Conducting multi-center trials helps to ensure that the study includes a sufficient number of subjects; that the subjects are properly representative of actual patient populations (geographic, racial and ethnic); and that the impact of any unrecognized biases of an investigator at a single center are minimized.

35. The elements of a placebo-controlled, randomized, double-blind clinical trial are generally as follows: A reliable clinical study to determine whether a product is effective in treating cancer must use objective criteria for patient selection and for measuring treatment outcomes. This is essential to obtaining meaningful data on the effect of the treatment in any strata of persons with cancer. It also is essential, because of differences in the causes of and treatments for the various types of cancer, that any clinical study to test the effect of a product on a specific type of cancer must be conducted on persons with that type of cancer.

36. In order to provide reliable evidence that a treatment actually has an effect, the study also receives a treatment which appears, in all ways possible, to be identical to the active treatment being studied, but which does not have any effect. The control group members should meet the same criteria as members of the treatment group. A placebo group is needed to measure the extent to which the subjects' participation in the study can cause a change or improvement in their condition independent of the treatment. Thus, the control group provides a basis for comparing what otherwise could be expected to happen to a similar population not receiving the active treatment over the same time period. Another acceptable study design is a direct comparison trial in which the experimental treatment is compared to another established treatment which has a well documented and reproducible effect. The goal of this study design is to determine if the experimental product is equivalent or superior to an established therapy.

37. The study must be "double-blinded," meaning that the study participants and the investigators who interact with the study patients cannot know whether a patient is in the active product or placebo group. Double-blinding is important to prevent patients and investigators from being influenced by a belief that a treatment will or will not be effective.

38. The study also must be randomized. Randomization is the method by which study patients are randomly assigned to either the active product group or the placebo group. The purpose of randomization is to insure that the researcher does not consciously or unconsciously employ a selection bias in assembling the active product and placebo groups. Proper randomization insures there is a statistical likelihood that members of the active product and placebo groups will be similar on all relevant characteristics.

39. In order for a study to support a particular claim, it must measure endpoints pertinent to that claim. Any study to determine whether a product is beneficial in treating cancer must, at a minimum, measure and record objective response by accepted criteria (such as RECIST) and toxicity by standard NCI adverse event reporting criteria during the study and at appropriate intervals. Well-designed trials to test potential new cancer treatments generally measure at least two different end points, such as disease response (complete remission, partial remission, stable disease, progression) and disease free or overall survival in all subjects. In brief, well-designed controlled clinical studies generally measure a treatment's effect on the cancer through the following types of tests:

A. Radiologic measurements such as computerized tomographic (CT) scans, magnetic resonance imaging (MRI), PET (positron emission tomography) scans, radionuclide scans, plain x-rays);

B. Blood tests for disease markers, such as beta-HCG and alpha-feto protein in testicular cancer and prostate specific antigen (PSA) in prostate cancer; and

C. Physical examination, endoscopic examination, biopsies, and other methods.

40. In most instances, a clinical study that is designed to produce reliable results should also: detail the inclusion and exclusion criteria for study participants; provide baseline, intermediate and final data for the relevant characteristics of the subjects; specify the procedures for collecting data from subjects, and all measures for monitoring subject compliance; specify how subject drop-outs and withdrawals are to be handled; and specify the precise means of measuring the primary and secondary endpoints related to determining whether the treatment had an effect. When studies fail to meet and/or disclose these criteria, the reliability of the study data is compromised.

41. Once a clinical trial is completed and all data are collected, the data for the treatment and control groups must be compared through the use of an appropriate statistical analysis, preferably conducted under the direction of a biostatistician. The treatment can only be said to have had an effect if the results of the treatment group are statistically significantly different from the results obtained by the placebo group. In addition, to demonstrate that a treatment has

an effect, the study results must be clinically significant. For instance, in order to demonstrate that a treatment has an effect on serum PSA levels, the effect shown must be sufficient to produce a clinically significant improvement in the patient's serum PSA levels.

42. It is generally not acceptable to rely upon clinical testing of one preparation to support the efficacy of another non-identical preparation. At a minimum, in order to state that clinical testing on one preparation *suggests* that another preparation is likely to be efficacious, experts would require scientific evidence showing that the second product contains the same active ingredients as the tested product, that the dosage(s) of the active ingredient(s) in the second product is in the appropriate range, and that the second product is absorbed and metabolized to the same extent as the first, through the same routes.

43. A study conducted on one product containing higher doses of the same ingredient than is contained in the second product would be insufficient to support a claim for the second product. Some products or substances may only be effective at or above a certain minimum threshold level. As a result, the fact that a study shows that a product or substance is efficacious at one dose does not show that it is efficacious at a lower dose.

44. Scientists also would not rely upon a study conducted on one product as evidence of the efficacy or safety of another product that contains other ingredients in addition to those in the tested product. Individual ingredients, which have been shown in one formulation to be safe or effective for the treatment of a specific condition, may have different properties when combined with other active ingredients. For this reason, a product that contains a combination of several potentially active ingredients must itself be tested through well-designed randomized controlled clinical trials in order to determine its efficacy in treating a given condition.

45. Anecdotal evidence of a product's effect, such as a report on the results of individual patients or a small group of patients, is not sufficient to demonstrate the efficacy of a product. While anecdotal evidence can be hypothesis generating, hypotheses must be carefully tested for the obvious reason that many do not prove to be accurate.

46. Animal studies are hypothesis-generating only and are not sufficient to demonstrate the efficacy of a product in humans. If an investigator obtains positive data through animal testing, that data can be an important factor in determining whether to pursue human studies. Likewise, while *in vitro* or cellular studies can be an important first step in testing a hypothesis, they are not sufficient to demonstrate the effect of a product in humans.

47. A competent and reliable placebo-controlled, randomized, double-blind trial to clinically prove that RAAX11 is effective in the prevention, treatment or cure of any cancer must show that subjects in the treatment groups had a statistically and clinically significant decrease in disease measurements, as compared to the placebo control groups. If a product such as RAAX11 is tested as an add-on to the subjects' existing cancer medications, then the control groups must receive both a placebo and their existing medications. Well-designed trials of cancer treatments will assess the product's effect on the cancer and the patient through measurements of tumor and treatment side effects, as detailed above, in order to ensure that any

effect seen in individual markers is due to a true effect on the disease and not simply an effect on one marker.

48. In order to demonstrate that a product such as RAAX11 can treat any kind of cancer, an adequate clinical comparison trial would require that RAAX11 be tested head-to-head against each proven cancer treatment about which the comparison claim is made. The number of subjects and centers sufficient to conduct such a study would depend upon several factors, including the number and types of cancer medications that RAAX11 is being tested against, the doses to be used, and the specific characteristics of the cancer patients on which it is to be tested. As discussed above, any such clinical study should evaluate multiple disease measurements and markers to determine if a true effect is shown by the treatment.

49. In order to demonstrate that a product such as RAAX11 can cure any kind of cancer, researchers would need to demonstrate through sufficiently large, well designed and reliably conducted randomized controlled trials that a statistically significant percentage of subjects in the experimental treatment groups, respectively, were able to attain normal marker levels and then maintain them for an extended period of time *after* subjects discontinued their use of RAAX11 and other cancer medications. To demonstrate a curative effect of RAAX11, it has to result in more people living for five years without disease relapse after the treatment is discontinued in the treatment compared to the placebo group.

V. Substantiation Provided by Respondents

50. I have reviewed each of the documents identified in Exhibit B to this declaration, which materials I am informed were provided to the FTC by the respondents in this action. These documents do not provide any data from randomized, placebo-controlled clinical trials with cancer patients. Therefore, these documents do not provide any additional relevant clinical data to substantiate or otherwise support the claims challenged by the FTC for the product RAAX11.

VI. Conclusion

51. As an expert in cancer research and a practicing medical oncologist, it is my opinion that based upon my knowledge, experience, and training in the treatment of cancer, my general knowledge of the scientific literature on the treatment of cancer, and my review of the materials discussed herein, it is my opinion that there is no reliable scientific evidence to support the claims that: A) Reliable scientific evidence demonstrates that RAAX11 is effective in the prevention, treatment, and cure of cancer; B) RAAX11 is effective in the treatment and cure of various types of cancer, including, but not limited to leukemia and cancers of the breast, brain, lung, larynx, pancreas, and bowel; and C) RAAX11 is effective in the prevention of cancer, including, but not limited to uterine cancer. Therefore, there is no reliable scientific evidence for any of the challenged claims for RAAX11.

Dated: 1/28/09

Omer Kucuk, M.D.

Attachment A

EMORY UNIVERSITY SCHOOL OF MEDICINE
CURRICULUM VITAE

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CURRENT TITLES AND AFFILIATIONS

ACADEMIC

2008 - Acting Professor of Hematology and Medical Oncology, Department of Hematology and Medical Oncology, Emory University School of Medicine

CLINICAL

2008 - Attending Staff, Emory University Hospital

2008 - Attending Staff, Emory Crawford Long Hospital

2008 - Attending Staff, Grady Memorial Hospital

2008 - Member, Genitourinary Multidisciplinary Team, WCI, Emory University

PREVIOUS ACADEMIC AND PROFESSIONAL APPOINTMENTS

1981 - 1984 Instructor, Department of Medicine, Section of Medical Oncology, Northwestern University Medical School, Chicago, Illinois.

1984 - 1988 Assistant Professor, Department of Medicine, Section of Oncology/Hematology, University of Health Sciences/The Chicago Medical School, North Chicago, Illinois.

1988 - 1991 Associate Professor, Department of Medicine, Section of Hematology/Oncology, University of Health Sciences/The Chicago Medical School, North Chicago, Illinois.

1991 - 1995 Professor, Department of Medicine, Section of Medical Oncology, University of Hawaii,

	John A. Burns School of Medicine, Honolulu, HI.
1991 - 1995	Researcher, Cancer Research Center of Hawaii, Prevention and Control Program, University of Hawaii at Manoa, Honolulu, Hawaii.
1992 - 1995	Faculty Member, Interdisciplinary Biomedical Sciences Graduate Program, University of Hawaii at Manoa, Honolulu, Hawaii.
1995 - 2008	Professor (tenured), Department of Internal Medicine, Division of Hematology and Oncology, Wayne State University, Detroit, Michigan.
1996 - 2008	Faculty Member, Cancer Biology Graduate Program, Wayne State University School of Medicine, Detroit, Michigan.
1997 – 2008	Professor, Barbara Ann Karmanos Cancer Institute, Detroit, MI.
1998 – 2008	Professor (adjunct), Department of Nutrition and Food Science, WSU
2000 – 2008	Professor, Department of Otolaryngology – Head and Neck Surgery, WSU

PREVIOUS ADMINISTRATIVE AND/OR CLINICAL APPOINTMENTS

1981 - 1984	Attending Physician, Northwestern Memorial Hospital and Northwestern Medical Faculty Foundation, Chicago, Illinois.
1981 - 1984	Attending Physician, Medical Service, Veterans Administration Lakeside Medical Center, Chicago, Illinois.
1984 - 1991	Attending Physician, Medical Service, Veterans Administration Medical Center, North Chicago, Illinois.
1989 - 1991	Consultant, Great Lakes Naval Hospital, Great Lakes, Illinois.
1989 - 1991	Associate Attending (Academic), Mt. Sinai Hospital Medical Center, Chicago, Illinois.
1992 - 1995	Attending Physician, Queen's Medical Center, Honolulu, Hawaii.
1992 - 1995	Attending Physician, St. Francis Medical Center, Honolulu, Hawaii.
1992 - 1995	Consultant Hematologist/Oncologist, Tripler Army Medical Center, Honolulu, Hawaii.
1993 - 1995	Attending Physician, Kuakini Medical Center, Honolulu, Hawaii.
1994 - 1995	Associate Chief for Research, Department of Oncology, Queens Medical Center, HI
1995 - 2008	Attending Staff Physician, Harper University Hospital, Detroit Medical Center, Detroit, Michigan.
1995 - 2008	Attending Staff Physician, Detroit Receiving Hospital, Detroit Medical Center, Detroit, Michigan.
1995 – 2008	Member, Head and Neck Cancer Multidisciplinary Team, KCI, WSU

1998 – 2000	Co-leader, Prevention Program, Karmanos Cancer Institute (KCI), WSU
2000 – 2003	Associate Leader, Population Sciences and Prevention Program, KCI, WSU
2002 – 2003	Leader, Prevention Program, KCI, WSU
2003 – 2008	Member, Population Sciences and Prevention Program, KCI, WSU
2003 – 2008	Member, Genitourinary Cancer Multidisciplinary Team, KCI, WSU

LICENSURE

Licenses: Michigan, 1976; Illinois, 1977; Hawaii, 1991; Georgia, 2008

SPECIALTY BOARD CERTIFICATION

Boards: American Board of Internal Medicine, 1978
Subspecialty of Hematology, 1984
Subspecialty of Medical Oncology, 1989

EDUCATION

1969 - 1975	MD, Hacettepe University Medical School, Ankara, Turkey

POSTGRADUATE TRAINING

1975 - 1978	Medical Internship and Residency, St. Francis Hospital, Evanston, Illinois
1978 - 1979	Hematology-Oncology Fellowship, St. Francis Hospital, Evanston, Illinois
1979 - 1981	Hematology-Oncology Fellowship, Northwestern University Medical School, Chicago, Illinois

COMMITTEE MEMBERSHIPS

NATIONAL AND INTERNATIONAL

1. Member: NCI Special Emphasis Panel. Program Project Applications for Chemoprevention Studies in High-Risk Populations, August 1997.
2. Member of AACR Program Committee, AACR Clinical Prevention Studies Section, Prevention Subcommittee, 1998.
3. Member: NCI Special Emphasis Panel. Phase I and Phase II Clinical Studies of Chemopreventive Agents. February-March 1999.
4. Member: NCI Special Emphasis Panel. Tobacco Use Research Center (P50) Applications. July 8-9, 1999.

5. Member: NCI Special Emphasis Panel. Phase II Chemoprevention Master Agreement Applications. August 12, 1999.

6. Member: NCI Special Emphasis Panel for Small Grants in Cancer Chemoprevention. July 18-19, 2000.

7. Member: NCI Special Emphasis Panel. Innovative Cancer Complementary and Alternative Medicine Initiative in Cancer Centers. February 19-21, 2001.

8. Member: US Department of Veterans Affairs (VA) Medical Research Service Merit Review Subcommittee for Oncology. Meets twice a year, 2001-2004.

9. Member: Site Visit Team, NIH Cancer Center Support Grant, University of California Irvine Cancer Center (Frank Meyskens, PI), Irvine, CA. January 26, 2002.

10. Member: NCI Special Emphasis Panel. Molecular targets for nutrients in prostate cancer prevention. November 19-20, 2002.

11. Member of Scientific Committee, International Meeting "Molecular Targets for Cancer Prevention Diagnosis and Treatment, Cyprus, October, 2007.

REGIONAL AND STATE

Eastern Cooperative Oncology Group (ECOG)

1983-1991	Toxicity Committee
1984-1991	Leukemia Committee
1984-1991	Lymphoma Committee
1984-1991	New Agents and Pilot Studies Committee
1986-1991	Cancer Control and Health Practices Committee
1986-1991	Biologic Response Modifiers Committee

Southwest Oncology Group (SWOG)

1991-	Head and Neck Cancer Committee
1991-	Cancer Control Research Committee
1991-	Genitourinary (GU) Cancer Committee
1992-	Chemoprevention Subcommittee (Co-Chairman 1993-1997)
1992-1997	Cancer Control Research Executive Committee
1998-	Lung Cancer Committee
1999-	CCRC Molecular Epidemiology Subcommittee
2000-	Lung Tumor Biology Subcommittee

Radiation Therapy Oncology Group (RTOG)

1998-	Chemoprevention Committee
1998-	Molecular Epidemiology Committee
1998-	Late Effects Committee
1998-	Head and Neck Committee
1998-	Medical Oncology Committee

INSTITUTIONAL

University of Health Sciences/The Chicago Medical School

1986-1991	Research & Development Committee
1987-1991	Institutional Review Board for Protection of Human Subjects
1988-1989	Academic Assembly Advisory Council
1988-1989	Student Admissions Committee

Veterans Administration Medical Center, North Chicago

1986-1989	Research Audit Committee (Chairman)
1987-1989	Human Subjects Committee
1987-1988	Quality Assurance Committee
1987-1991	Transfusion Committee
1987-1989	Tissue Committee

Illinois Cancer Council, Chicago, Illinois

1987-1991	Clinical Trials Executive Committee
1987-1991	Hematology Committee (Chairman)
1987-1991	Biologic Response Modifiers Committee
1987-1991	Head and Neck Committee
1988-1989	Board of Trustees

Cancer Research Center of Hawaii, Honolulu, Hawaii

1991-1995	Clinical Steering Committee
1992-1993	Executive Committee
1992-1993	Research Medical Oncologist Search Committee (Chairman)
1992-1993	American Cancer Society Institutional Grant Review Committee
1992-1993	Internal Planning Committee
1992-1995	Clin. Oncology Research Career Development Prog. Advisory Committee
1993-1995	Clinical Protocol Review Committee
1993-1995	Shared Resource for Clinical Data Base Management (Coordinator)

University of Hawaii at Manoa, Honolulu, Hawaii

1993-1995	Committee on Human Studies (Ad Hoc Committee Member)
1993-1995	Department of Medicine Residency Program Oversight Committee (John A. Burns School of Medicine & Queen's Medical Center)
1993-1995	Assistant Director of Medical Education (John A. Burns School of Medicine, Department of Medicine)

Queen's Medical Center, Honolulu, Hawaii

1993-1995	Cancer Committee
1993-1995	Cancer Institute Board

St. Francis Medical Center, Honolulu, Hawaii

1994-1995	Institutional Review Board for Human Subjects
1994-1995	Institute of Cancer Administrative Committee
1994-1995	Institute of Research, Administrative Committee

Kuakini Medical Center, Honolulu, Hawaii

1994-1995	Research Committee
1994-1995	Oncology Committee

Harper Hospital, Detroit, Michigan

1995	Morbidity and Mortality Committee
1995	Medication Use Committee

Karmanos Cancer Institute, Detroit, Michigan

1995-1998	Leader, Primary Prevention Task Force, Cancer Control, Epidemiology and Environmental Carcinogenesis Program
1996-2004	Head, Cancer Prevention Research, Division of Hematology Oncology
1997	Member (Ad Hoc), Clinical Trials Quality Assurance Committee
1998-2004	Leader, Cancer Prevention Research
	Protocol Review and Monitoring Committee
1999-	Co-Leader, Population Sciences and Prevention Program
2000-2004	Leader, Prevention Program
2004-	Member, Population Sciences and Prevention Program
2006-	Member, Promotions and Tenure Committee

Wayne State University, School of Medicine, Detroit, Michigan

2000-2001	Human Investigations Committee
2005-2007	Department of Internal Medicine Tenured P&T Committee

2007-2008 Research and Development Committee

CONSULTANTSHIPS

1999	Member Scientific Advisory Board, Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease
2003	Member Scientific Advisory Board. Fifth International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, 2003

EDITORSHIPS AND EDITORIAL BOARDS

2000-	Editorial Board: Annals of Medical Sciences
2002-	Editorial Board: Cancer Epidemiology, Biomarkers and Prevention
2002-	Editorial Board: Turkish Journal of Cancer
2003-	Editorial Board: International Journal of Hematology and Oncology
2005-	Editorial Board: Advances in Molecular Medicine
	Guest Editor: Cancer and Metastasis Reviews
2007-	Assistant Editor: Cancer Detection and Prevention

MANUSCRIPT REVIEWER

Cancer
Otolaryngology
Free Radical Biology & Medicine
Oncology
Urology
Nicotine and Tobacco Research
Cancer Control
Cancer Epidemiology Biomarkers and Prevention
Nutrition and Cancer
The Journal of Urology
Cancer Investigation
Cancer Detection and Prevention
Lung Cancer
Genetics
Clinical Cancer Research
Cancer Research
Cancer Gene Therapy
Asian Journal of Andrology
Cell Biology and Toxicology
Ethnicity and Disease
Molecular Cancer Therapeutics
PNAS
FEBS Letters
Cancer Cell International
Recent Patents on Endocrine, Metabolic & Immune Drug Discovery
Journal of Medicinal Food
Molecular Nutrition and Food Research
Head and Neck

HONORS AND AWARDS

1998	College Teaching Award, Wayne State University
2000	President's Achievement Award for Community Research, Karmanos Cancer Institute
2000	President's Achievement Award for Outstanding Service, Karmanos Cancer Institute
2000	Faculty Research Excellence Award, School of Medicine, Wayne State University
2001–2002	Best Doctors in America®
2002	College Teaching Award, Wayne State University
2003-2004	Best Doctors in America®
2005-2006	Best Doctors in America®
2006	College Teaching Award, Wayne State University
2006	America's Top Physicians
2007-2008	Best Doctors in America®

PROFESSIONAL SOCIETY MEMBERSHIPS

American Society of Clinical Oncology
American Association for Cancer Research
American Society of Preventive Oncology
American Society for Nutrition
American College of Nutrition (Fellow)
American Urological Association
Society for Free Radical Biology and Medicine
American Head and Neck Society
Society of Basic Urological Research

ORGANIZATION OF NATIONAL OR INTERNATIONAL CONFERENCES

2003	International Soy Symposium Advisory Committee, Orlando, Florida. (9/20/03-9/23/03)
2005	Session Chairman and Organizer (Soy and Cancer Therapy) at the Annual Meeting of American College of Nutrition. 9/22/05 - 9/25/05
2008	Organizer: Chairman, First International Nutrition and Cancer Congress, Antalya, Turkey; May 19-23, 2008 (www.nutritioncancer2008.org) Due to the meeting success, the second meeting will be organized in 2009.

RESEARCH FOCUS

My research focuses on the use of clinical trials in appropriate populations to demonstrate the efficacy and mechanisms of cancer preventive compounds in humans. Biomarkers of cancer risk and progression are used as intermediate endpoints and their modulation by chemopreventive agents are demonstrated in small clinical studies prior to the initiation of larger phase III clinical trials. Current investigations focus on the effects of micronutrients and phytochemicals on biomarkers of cell proliferation, differentiation, apoptosis and oxidative stress in a variety of cancers. I also investigate the modulation of genetic and epigenetic pathways of carcinogenesis by nutritional interventions.

GRANT SUPPORT

ACTIVE SUPPORT

1. University of Michigan Head and Neck SPORE (PI: Wolf, Gregory) "The Molecular Basis of Head and Neck Cancer Biology, Treatment and Prevention", NIH #2P50CA-097248-06A1 (2002-2013); Co-Investigator on project: Role of Soy Isoflavones, Smoking Abstinence and Molecular Markers in Prevention (Project total $608,339) NIH #2P50CA097248-06A100008, 07/01/2008 – 07/30/2013. SPORE Total $12,992.599
   Note: I am a co-investigator on this SPORE; since the work is done in Michigan, I receive no funding

PREVIOUS SUPPORT

1. Chicago Medical School Biomedical Research Support Grant Program; Principal Investigator; "Effects of Oxygenated Sterols on Tumor Cell Killing by Lymphocytes".; 4/85-3/86; $3,400

2. Veterans Administration Regional Advisory Group; Principal Investigator; "Effects of Oxygenated Sterols on Tumor Cell Killing Lymphocytes".; 4/86-3/87; $27,000

3. Bionetics Research Institute Contract; Principal Investigator; "Active Specific Immunotherapy in Colon Cancer ECOG EST 5283".; 1987-1991; $10,000 per year.

4. NIH #1 S10 RR03432-01; Co-Principal Investigator; Flow Cytometry System Equipment, BRS Shared Instrumentation Grant from Division of Research Resources.; 2/87-2/88; $176,000

5. Illinois Cancer Council; Principal Investigator; "Chicago Medical School Clinical Cancer Research Program.; 7/87-6/88; $5,000

6. Illinois Cancer Council; Principal Investigator; "Effects of Oxygenated Sterols on Tumor Cell Killing Lymphocytes".; 11/87-10/88; $13,200

7. NIH #1 U10 CA 1414416; Co-Principal Investigator; "Eastern Cooperative Outreach Group (ECOG) (Frontier Science and Technology Research Foundation, Inc.)".; 12/87-11/88; $35,744

8. NIH #5 U10 CA 1414416; Co-Principal Investigator; "Eastern Cooperative Group Outreach Group (ECOG)"; 5/88-4/89; $77,625

9. Chicago Medical School Biomedical Research Support Grant Program #BRSG S07 RR05266-27; Principal Investigator; "Effects of Oxysterols on NK Cell Activity and Specific CMC"; 11/88-3/89; $3,000

10. Veterans Administration Merit Review Board #MRB TAB No.15; Co-Principal Investigator; "Effects of Oxysterols in Sickle Red Cells".; 4/89-3/92; $221.100

11. Hoffman-LaRoche; Principal Investigator; "A Phase III Open, Randomized Trial Comparing Roferon-A and Hydroxyurea in Patients with Ph-1 Positive Chronic Myelogenous Leukemia"; 1989-1991; $9,345

12. Janssen Pharmaceuticals; Principal Investigator; "Liarazole vs. Prednisone in the Treatment of Relapsed Prostate Cancer"; 1993-1996; Approximately $83,000 per year

13. NCI #2 RO1 C45504-05 A1; Co-Investigator (Subcontract); Principal Investigator, Ernst Wynder; "Women's Intervention Nutritional Study"; 1993-1996; Approximately $55,000 per year.

14. Hoffman-LaRoche; Co-Investigator; Principal Investigator, John Bertram; "Carotenoids and Human Health";

1993-1994; $27,000

15. NCI #R01; Co-Investigator, 25% effort; Principal Investigator, B.F. Issell; "Breast Cancer Treatment Protocols for Hawaii Minorities".; 7/1/94-6/30/97; $631,637

16. NCI #R01; Co-Investigator; PI, Loic LeMarchand; "Dietary Intervention Trial for Lung and Head and Neck Cancers"; funded 1993-1998; $550,384/year.

17. NIH UO1; Co-Investigator; Principal Investigator, Zora Djuric; "Dietary Intervention in Women at High Risk for Breast Cancer"; funded 1/1/97-12/31/01; total cost $1,925,996; direct cost $322,223/year.

18. Cancer Treat. Res. Foundation; Principal Investigator; "Zinc supplementation in head and neck cancer"; funded 11/1/97-5/31/01; total cost $160,212.

19. Virtual Discovery, KCI; Principal Investigator; "In vitro and in vivo modulation of prostate cancer cell growth and differentiation by lycopene"; funded 3/1/97-3/31/99; total cost $70,295.

20. Eli Lilly and Company: Principal Investigator: Phase II study of GEMTAX in previously treated head and neck cancer. Funded: total cost $83,000. (3/98-3/01)

21. NIH R21: Co-investigator; "Zinc Supplementation Trial in Head and Neck Cancer" Ananda Prasad (PI); funded 4/1/98-3/31/01;$195,630 total direct cost.

22. VA Merit; Co-Principal Investigator; "Prevention of colorectal adenoma recurrence by folate" Adhip Majumdar, Ph.D., PI; funded: 10/1/98 - 9/30/03; total cost ~$500,000.

23. KCI Virtual Discovery; Co-Investigator: Effect of tobacco cessation on oxidative stress markers. Funded: $20,000, 5/1/99-4/30/01.

24. KCI Virtual Discovery; Principal Investigator: Effect of zinc supplementation on oxidative stress markers. Funded: $20,000, 5/1/99-4/31/03.

25. Eli Lilly and Company; Principal Investigator: GEMTAX for previously untreated advanced head and neck cancer. Total cost $100,000. Funded 2001-2005.

26. Eli Lilly and Company; Principal Investigator: GEMDOC for previously treated SCCHN. Total cost $100,000.Funded 2005-2008.

27. NIH/SWOG; Principal Investigator: WSU SWOG Prevention Program. $49,218/year.

28. NIH P30 Cancer Center Support Grant; John D. Crissman, MD, PI; Co-Leader, Population Sciences and Prevention Program. Funded 12/1/00 – 11/30/02; 5% effort.

29. LycoRed; Principal Investigator; Lycopene and Soy Isoflavones in Advanced prostate Cancer. 2/1/01 – 3/1/06; $77,700.

30. Department of Defense 17-98-1-89353: Principal Investigator; "Modulation of Growth And Differentiation in Breast Cancer By Soy Isoflavones"; funded 10/1/98-9/30/03; total cost $742,000.

31. NIH competitive Contract N01-CN-85083-57: Principal Investigator: "A Phase II Clinical Trial of Soy Isoflavones in Patients with Clinically Localized Prostate Cancer: Modulation of Intermediate Endpoints". Funded 10/1/98-9/30/03; total direct cost $400,020; total cost $551,527.

32. NIH competitive Contract N01-CN-0502257; Principal Investigator: "Phase IIb Trial of Zileuton in Persons

with Bronchial Dysplasia. 4/1/01-9/30/06; total direct cost $1,402,882; total cost $1,729,026; 10% effort.

33. Sanofi-Aventis. Investigator Initiated. Principal Investigator, 5% effort. Phase II Study of Gemcitabine and Docetaxel in Previously Untreated Head and Neck Cancer. 10/1/04 - 9/1/08. Total $100,000. (investigator initiated)

34. Komen Foundation. Co-investigator. 5% effort. Sound speed measurement of the breast: A novel approach to assessing breast density and cancer risk. (Neb Duric, PI, 9/1/06 – 8/31/07. Total $112,875.

CLINICAL SERVICE CONTRIBUTIONS

COMMUNITY SERVICE

1. Talked at the monthly meeting of the Farmington Rotary Club. Topic: Cancer Prevention. August 29, 1995. (Judy Schwartz, host)
2. Two TV interviews with Channel 2 Health Correspondent; Topics: "Garlic and Health" and "Phytochemicals and Health". 1995.
3. Two Channel 4 TV Interviews regarding "Effects of Tobacco on the Lungs" and "Tobacco and Cancer". 1996.
4. Channel 7, WXYZ, Interview by Jerry Hodak on 2/18/97, broadcast multiple times: "Clinical Study of Vitamin E in the Prevention of Oral Cancer"
5. Channel 2: Vitamin E and Health. May 13, 1997.
6. Multiple TV interviews in 1997 and 1998 on various nutrients and cancer (lycopene and prostate cancer, isoflavones and breast cancer, retinoids, etc).
7. Multiple radio (WWJ AM 950) and magazine (Readers Digest 8/98, Prevention 1/99, Better & Better Magazine for Seniors) interviews on nutrition and cancer.
8. Channel 2: Lycopene and prostate cancer prevention. August 4, 1998.
9. Numerous TV, radio and newspaper interviews on nutrition and cancer.
10. Karmanos Cancer Institute Volunteer Leadership Celebration meeting. Fusion Restaurant, Farmington Hills, Michigan. Talk on "Diet and Cancer Prevention". September 30, 1999.
11. Talk: Soy in Cancer Prevention. Taubman Jewish Community Campus, Oak Park, Michigan. Made a 1 hour slide presentation on cancer preventive properties of soy isoflavones, presented scientific evidence in lay language and answered questions. Tuesday 3/28/00. 7:30-9:00 pm.
12. Talk: Diet, soy, lycopene and cancer. Daimler-Chrysler. Introduced by Susan Weinberger, Head of Health Education, Community Outreach Program, KCI. Audience ~150-200 Daimler Chrysler Employees or former employees. May 3, 2000. 10:30 – 11:30 am. Location Daimler-Chrysler Training Facility, East Jefferson Avenue, Detroit, MI.

PATIENT CARE

1. Inpatients (2-5 patients/day) and consults (2-4/week) seen daily at Karmanos Hospital (4-8 chemotherapy admissions per week). (1995 – 2008)
   Outpatients seen at Wertz Clinical Cancer Center 4 half days per week (average 30 return patients,
2. 3-6 new patients per week) (1995 – 2008)
3. Patients seen at the Multidisciplinary Head and Neck Special Clinic at the Wertz Clinical Cancer Center, Wednesdays between 10:30 and 11:30. (1995 – 2008)
4. Patients seen in consultation at the Detroit Receiving Hospital during Oncology Teaching Service (3-4 per wk) (2-4 weeks per year) (1995 – 2008)
5. Patients seen for Medical Oncology Service (4-6 weeks per year). (1995 – present)

CLINICAL STUDY PROTOCOLS (CHAIRMAN, CO-CHAIRMAN OR MONITOR)

Eastern Cooperative Oncology Group

1. Study Chairman, EST P-A185 (Completed), Pilot Study of Cisplatin and 5-FU in Previously Treated Metastatic Breast Carcinoma
2. Study Chairman, EST P-B586 (Completed), Phase II Pilot Study of Cisplatin, 5-FU and VP-16 for Advanced Non-Small Cell Lung Cancer
3. Study Co-Chairman, EST P-B287 (Completed), Phase II Study of Etoposide, Doxorubicin, and Cisplatin in Patients with Advanced Gastric Cancer
4. Study Chairman, EST 1489 (Completed), Phase II Study of Didemnin B (NSC 325319) in Previously Treated Non-Hodgkin's Lymphoma

Illinois Cancer Center

1. Study Chairman, ICC 86H1 (Completed), Phase II Evaluation of Menogaril in Previously Treated Multiple Myeloma
2. Study Monitor, ICC 83H2 (Completed), Phase II Study of ATDA in Advanced Non-Hodgkin's Lymphoma
3. Study Monitor, ICC 89L1 (Completed), Phase II Study of New Agents in Treatment of Incurable Small Cell Carcinoma of Lung (ATDA)
4. Study Monitor, ICC 89L2 (Completed), Phase II Study of Merbarone for Advanced Non-Small Cell Lung Cancer

Cancer Research Center of Hawaii

1. Study Chairman, CRCH 9105 (closed), Pilot Trial of Beta Carotene and Vitamin E in Chemoprevention of Second Malignancies in Patients with Cured Squamous Cell Carcinomas of Head and Neck: An Intermediate Endpoint and Feasibility Study
2. Study Co-Chairman, CRCH 9201 (Completed), Biomarker Studies in Healthy Volunteers
3. Study Chairman, CRCH 9204 (Active), Women's Intervention Nutrition Study (WINS)
4. Study Chairman, CRCH 9205 (closed), Chemoprevention of Superficial Bladder Cancer Recurrence
5. Study Co-Chairman, CRCH 9210 (Completed), Liarazole vs. Prednisone in the Treatment of Relapsed Prostate Cancer
6. Study Chairman, CRCH 9303 (Completed), Biomarkers of Genotoxicity and Oxidative Damage in Healthy Adults: Modulation by beta-carotene and alpha-tocopherol
7. Study Co-Chairman, CRCH 9302 (Active), Dietary Intervention Trial Among Lung and Head and Neck Cancer Patients
8. Study Chairman, CRCH 9307 (closed), Effects of B-carotene and A-tocopherol on Blood Levels of Cholesterol oxides in Cancer Patients after Curative Radiation
9. Study Chairman, CRCH 9310 (closed), Beta-carotene Supplementation and its Effect on Breast Tissue
10. Study Chairman, CRCH 9402 (closed), Oxysterols and Connexin in Benign and Cancerous Prostate
11. Study Chairman, CRCH 9403 (closed), Dietary Fat and Plasma Cholesterol Epoxides in Breast Cancer
12. Study Co-Chairman, CRCH 9406 (completed), Appropriateness of Recommended Treatments for Patients with Breast Cancer

Southwest Oncology Group

1. Study Chairman, SWOG 9235 (Completed), Phase II Trial of Casodex in Prostate Cancer Patients who Failed Conventional Hormonal Manipulation
2. Study Chairman, SWOG 9507 (S-1617) (Closed), Phase II Study to Determine the Safety and Efficacy of 4-HPR (N-(4-Hydroxyphenyl) Retinamide) for Treating Oral Intraepithelial Neoplasia.
3. Study Co-chairman, SWOG 9908, A Double-blind, Placebo-controlled Trial to Study the Efficacy ad Safety of Glutamine Supplementation upon Radiation Therapy Induced Oral Mucositis in Head and Neck Cancer Patients (S. Klimberg, PI)
4. Study Co-Chair, E5597-Intergroup, Prevention of second primaries with selenium in stage I non-small cell lung cancer. (D. Karp, PI)
5. Study Chair, Phase II Study of Gemcitabine and Paclitaxel in Previously Treated Head and Neck Cancer.
6. SWOG Study Chair, Soy supplementation prior to head and neck surgery: Modulation of biomarkers of growth and differentiation (LOI accepted).

Karmanos Cancer Institute/Wayne State University

1. Study Chair (C-1275), Treatment of Oral Squamous Intraepithelial Neoplasia with Alpha-tocopherol
2. Study Co-chair (D-1150), Cisplatin, Taxol and 5-FU in Patients with Advanced Head and Neck Cancer (Maha Hussain, chair)
3. Co-Investigator (SWOG PI). (C-2327) E5597, Intergroup Phase III Randomized Placebo Controlled Trial of Selenium in Stage I Non-Small Cell Lung Cancer.
4. Principal Investigator. SWOG-9507. Phase II Study to Determine the Safety and Efficacy of 4-HPR [N-(4-Hydroxyphenyl) Retinamide; Fenretinide] for Treating Oral Squamous Intraepithelial Neoplasia. CLOSED.
5. Co-Investigator. SWOG 9908, A Double-blind, Placebo-controlled Trial to Study the Efficacy and Safety of Glutamine Supplementation upon Radiation Therapy Induced Oral Mucositis in Head and Neck Cancer Patients.
6. Principal Investigator. Phase II Study of Gemcitabine and Paclitaxel in Previously Treated Head and Neck Cancer. Local Protocol (D-1633). Supported by a grant from Eli Lilly and Company.
7. Co-Investigator. Phase II Study of Gemcitabine and Paclitaxel in Advanced Non-Small Cell Lung Cancer. A. Wozniak, PI. Local Protocol (D-1478). Supported by a grant from Eli Lilly and Company.
8. Principal Investigator. Modulation of Growth and Differentiation in Breast Cancer by Soy Isoflavones. Local Protocol (D-1458). Supported by a grant from the Department of Defense.
9. Principal Investigator. Zinc Supplementation Trial in Stage III-IV Head and Neck Cancer Patients Treated With Radiation Therapy. Local Protocol (D-1684). Supported by a grant from Cancer Treatment Research Foundation.
10. Co-Principal Investigator. Zinc Supplementation Trial in Stage III-IV Head and Neck Cancer Patients Treated with Radiation and Cisplatin Therapy. Local protocol (D-1477). A. Prasad, PI. Supported by a grant from the NIH (R21).
11. Co-Principal Investigator. (D-1671), Phase I-II Trial of Intra-operative cisplatin and 5-fluorouracil in advanced head and neck cancer. (J. R. Jacobs, PI)
12. Principal Investigator (D-1660), Gemcitabine and Paclitaxel in Previously Untreated Advanced H&N Cancer. Funded by a grant from Eli Lilly.
13. Principal Investigator (D-1631), Soy Isoflavone in the Prevention of Prostate Cancer. Supported by a grant from the NIH.
14. Principal Investigator (C-2325), Soy isoflavones in patients receiving radiation therapy for localized prostate cancer.
15. Principal Investigator (C-2418), Multidose randomized trial of soy isoflavones in patients with localized prostate cancer prior to prostatectomy. Supported by a grant from the NIH.
16. Principal Investigator (C-2405), Zileuton in the treatment of bronchial dysplasia. Supported by a grant from the NIH.
17. Principal Investigator (C-2326), Lycopene and soy isoflavones in the treatment of advanced prostate cancer. Supported by a grant from LycoRed, Beer-Sheva, Israel.
18. Principal Investigator (D-2600), Modulation of growth and differentiation in breast cancer by soy isoflavones and tamoxifen.
19. Co-Investigator, Gemcitabine and soy isoflavones in advanced breast cancer. (Philip Philip, MD, PI)
20. Co-Investigator, Phase II study of DIM in prostate cancer. (Elisabeth Heath, MD, PI)

ADDITIONAL SERVICE AT WAYNE STATE UNIVERSITY/KARMANOS CANCER INSTITUTE/DETROIT MEDICAL CENTER:

1. Member, Medication Use Committee, Harper Hospital, monthly meetings, 7:30-9:00. (1995 – 2008)
2. Member, Morbidity and Mortality Committee, Harper Hospital, monthly meetings, 7:30-9:00, April-June, 1995.
3. Member, Translational Research (Community) Task Force, Michigan Cancer Foundation, several meetings in July and August, 1995.
4. Leader, Primary Prevention Task Force, Cancer Control: Epidemiology and Environmental Carcinogenesis Program, Karmanos Cancer Institute. (1995 – 1998)
5. Interview faculty candidates for various departments. (1995 – 2008)

6. Head and Neck Cancer Service Meetings, Mondays 8:00-8:30 (1995 – 2008)
7. Head and Neck Multidisciplinary Conference, weekly. (1995 – 2008)
8. Head and Neck Multidisciplinary Clinic, weekly. (1995 – 2008)
9. Leader, Cancer Prevention Research, Karmanos Cancer Institute. (1998 – 2004)
10. KCI Prevention Research Meetings, monthly. (2000 – 2004)
11. Member, Search Committee for Director of Clinical Research. 2003
12. Member, Advisory Committee for R25 Training Grant in Cancer Prevention and Control (Sam Brooks, PhD) 2003
13. Research Liaison, Prevention Centers of Karmanos Cancer Institute. (2003 – 2004)
14. KCI Population Sciences and Prevention Program Administrative meetings, every two weeks. (2003 – 2004)
15. WSU Human Investigations Committee, monthly meetings, 3 hours. (2004 – 2005)

FORMAL TEACHING

Wayne State University/Detroit Medical Center

1. Oncology Service Teaching Attending: Harper and Detroit Receiving Hospitals May 1995, April 1996, November 1996, September 1997, November 1998, August 2001, December 2002.

2. Oncology Resident Outpatient Teaching: Every Friday at the Wertz Clinic

3. Hematology-Oncology Resident Lectures : Every 2-3 months; (Title: Head and Neck Cancer) 1995-1997.

4. Hematology-Oncology Fellows Conference: Lecture on Cancer Prevention (4/98)

5. Hematology-Oncology Fellows Journal Club: Twice in 4/98.

6. Faculty Advisor/Mentor for Oncology Fellows: Dr. Shabbir Ahmed (1995-96); Dr. Sucharu Prakash (1997-1999). Outpatient clinic teaching weekly. Dr. Ahmed (Trenton MI) and Dr. Prakash (Paris, TX) are currently private practice oncologists.

7. Lecturer, CB 711 Cancer Biology Survey Course (Director, Drs. Heppner, Pauley, Djuric). Graduate Program in Cancer Biology. Wayne State University School of Medicine. Lecture Title: Cancer Prevention. Dates: December 11, 1995; December 9, 1996; December 8, 1997; April 22, 1999.

8. Director and Lecturer, CB725, Cancer Prevention & Control Course: (2 credits)
Graduate Program in Cancer Biology. Winter Semester, 2 hours weekly, January to May. Organizes the course; develops the curriculum; prepares, administers and grades exams; gives 2-4 lectures; helps students individually when necessary.

9. Lecturer, NUR 820, Section 62808, Integration of Biological and Nursing Sciences: Theoretical Paradigms and Empirical Issues, Chandice Covington, Ph.D., R.N., Course Director. Lecture Title: Cancer Chemoprevention. Spring/Summer Semester 1996.

10. Attending Oncologist for Fellow's Clinic:
June 1996, October 1996 Wednesdays 9:00 to 13:00, 4 hours/week. Patients are seen, examined and discussed with fellows. Staff notes placed in charts.

11. Physical Diagnosis: Weekly, Thursdays 9:00 to 12:00, February 6 through May 1, 1997; weekly, Tuesdays 9:00 to 12:00, March 3 through May 1, 1998.

12. Lecture to Physician Assistant Students: Title: Head & Neck Cancer, 11/4/97, December 10, 1998, November 1999.

13. Professor Rounds: Grace Hospital, November 11, 1997.
Detroit Receiving Hospital, March 18, 1998.
Harper Hospital, January 27, 1999.
Detroit Receiving Hospital, November 24, 1999.

14. Oncology Fellows' Head & Neck Cancer Rotation: outpatients, consults, journal club.

SUPERVISORY TEACHING

Theses/Dissertations Directed

1. **Michael W. Rooney**, Ph.D. Thesis, Biomedical Engineering, Northwestern University, Evanston, IL: "Effects of cholesterol and its oxidized derivatives in lipid bilayers and erythrocyte membranes", June 1985. (Co-advisor with John W. Kauffman, Northwestern University).

2. **Sandy B.Y. Chin**, Ph.D. Thesis, Psychology, University of Health Sciences/The Chicago Medical School, North Chicago, IL: "Variables contributing to anticipatory nausea and vomiting in cancer chemotherapy", June 1987. (Co-advisors: Rolf Peterson, Ediz Ezdinli)

3. **Renee Szostek**, M.S. Thesis, Biomedical Engineering, Northwestern University, Evanston, IL: "Effects of oxysterols on normal and sickle red cell membranes", May 1990. (Co-advisors: Leonard J. Lis, John W. Kauffman and M.P. Westerman).

4. **Cynthia T. Aller**, Ph.D. Thesis, Microbiology and Immunology, University of Health Sciences/The Chicago Medical School, North Chicago, IL: "T, Tn antigen expression in lymphocytic leukemias", April 1993. (Co-advisors: Alice Gilman-Sachs and Georg Springer).

5. **Joanne Davis**, Ph.D. Thesis, Cancer Biology Program, Wayne State University, Detroit, MI: "Molecular Mechanisms of Growth Inhibition in Prostate Cancer by Soy Isoflavones" (Principal advisor: Fazlul Sarkar, Ph.D.; Co-advisors: Omer Kucuk, Ray Novak, Kaladhar Reddy), 2001.

6. **Gang Chen**, Ph.D. Thesis, Cancer Biology Program, Wayne State University, Detroit, MI: 2,6 cyclolycopene-1,5-diol: A new marker of oxidative stress. (Principal advisor: Zora Djuric, Ph.D.; Co-advisors: Omer Kucuk, Jeff Evelhoch, David Klurfeld), 2002.

7. **Julian Raffoul**, PhD Thesis: Effect of age on oxidative DNA damage and repair. Department of Nutrition and Food Science, Wayne State University, Detroit, MI. (Advisor: Ahmad Heydari; committee members: Omer Kucuk, David Klurfeld, Thomas Fungwe)

8. **Zhiwei Wang,** PhD Thesis: Regulation of NOTCH-1 signaling pathway by chemopreventive polyphenols. Department of Pathology (Advisor: Fazlul Sarkar, PhD; co-advisors: Omer Kucuk, Adhip Majumdar, Josh Liao)

Masters Thesis Essays directed:

1. MS BMS Program Student Thesis Essay Committee Member: Hakan Koymen (1997)

2. MS BMS Program Student Thesis Essay Committee Member: Fangru Lian (1998)

3. MS BMS Program Student Thesis Essay Advisor: Louis Kusnier (1998)

4. MS BMS Program Student Thesis Essay Advisor: Richard Berri (1998)

5. MS BMS Program Student Research Advisor: Rajesh Menon (1998)

6. MS BMS Program Student Research Advisor: Zafar Shamoon (1998)

7. MS BMS Program Student Research Advisor: Fathimazohare Syed (1999)

8. MS BMS Program Student Research Advisor: Vijay Khilanani (1999)

9. MS BMS Program Student Thesis Essay Advisor: Fathimazohare Syed (1999)

10. MS BMS Program Student Thesis Essay Advisor: Rajesh Menon (1999)

11. MS BMS Program Student Thesis Essay Committee Member: Dawn Geisler (1999)

12. MS BMS Program Student Thesis Essay Advisor: Arvind Surendran (2000)

13. MS BMS Program Student Thesis Essay Advisor: Emre Conklu (2000)

14. MS BMS Program Student Thesis Essay Advisor: Iftekhar Ahmad (2001)

15. MS BMS Program Student Thesis Essay Advisor: Tara Klix (2001)

16. MS BMS Program Student Thesis Essay Advisor: Lisa Ceravalo (2001)

17. MS BMS Program Student Thesis Essay Advisor: Dan Pechacho (2001)

18. MS BMS Program Student Thesis Essay Advisor: Jessica Parker (2001)

19. MS BMS Program Student Thesis Essay Advisor: Christopher Budziak (2002)

20. MS BMS Program Student Thesis Essay Advisor: Tamara Kamash (2002)

21. MS BMS Program Student Thesis Essay Advisor: Tamer Kamash (2002)

22. MS BMS Program Student Thesis Essay Advisor: Gregory Karapetian (2002)

23. MS BMS Program Student Thesis Essay Advisor: Rachelle Rivera (2002)

24. MS BMS Program Student Thesis Essay Advisor: Nichole Urban (2002)

25. MS BMS Program Student Thesis Essay Advisor: Brad Kremer (2002)

26. MS BMS Program Student Thesis Essay Advisor: Meaghan Nichol (2008)

LECTURESHIPS, SEMINAR INVITATIONS, AND VISITING PROFESSORSHIPS

1. **Kucuk, O**. Multiple Myeloma. Grand Rounds. Department of Medicine, Northwestern University School of Medicine, Chicago, IL, 1981.

2. **Kucuk, O**. Cancer Hypercoagulability. Grand Rounds. Department of Medicine, University of Southern Alabama School of Medicine, Mobile, AL, 1983.

3. **Kucuk, O**. Hypogammaglobulinemia. Grand Rounds. Department of Medicine, Edgewater Hospital, Chicago, IL, 1986.

4. **Kucuk, O**. Non-Hodgkin's Lymphoma. Grand Rounds. Department of Medicine, University of Health Sciences/The Chicago Medical School, North Chicago, IL, February 18, 1987.

5. **Kucuk, O**. Current Concepts in the Diagnosis and Management of Multiple Myeloma. Grand Rounds. Department of Medicine, University of Health Sciences/The Chicago Medical School, North Chicago, IL, September 14, 1988.

6. **Kucuk, O**. Multiple Myeloma. Grand Rounds. Department of Medicine, Edgewater Hospital, Chicago, IL, October 6, 1988.

7. **Kucuk, O**. Carcinoma of the Breast. Grand Rounds. Department of Medicine, University of Health Sciences/ The Chicago Medical School, North Chicago, IL, March 8, 1989.

8. **Kucuk, O**. Multiple Myeloma. Grand Rounds, Department of Medicine, Mount Sinai Hospital, Chicago, IL, November 26, 1989.

9. **Kucuk, O**. Chemoprevention. Research Seminar. Cancer Research Center of Hawaii, University of Hawaii at Manoa, Honolulu, HI, July 1, 1991.

10. **Kucuk, O**. Oxysterols. Research Seminar. Cancer Research Center of Hawaii, University of Hawaii at Manoa, Honolulu, HI, March 23, 1992.

11. **Kucuk, O**. Oxysterols as Intermediate Markers in Lung Cancer. Research Seminar. The Section of Head and Neck and Thoracic Medical Oncology, M.D. Anderson Cancer Center, Houston, TX, April 8, 1992.

12. **Kucuk, O**. Role of Oxysterols in Cancer and Heart Disease. Research Seminar. Division of Medicinal Chemistry and Pharmaceutics, College of Pharmacy, University of Kentucky, Lexington, KY, October 14, 1992.

13. **Kucuk, O**. Cancer Chemoprevention. Grand Rounds. Castle Medical Center, Kailua, HI, January 19, 1993.

14. **Kucuk, O**. Can We Really Prevent the Common Cancers? Grand Rounds. Castle Medical Center, Kailua, HI, November 23, 1993.

15. **Kucuk, O**. Biomarkers of Cancer Susceptibility. Research Seminar. Cancer Research Center of Hawaii, University of Hawaii at Manoa, Honolulu, HI, December 6, 1993.

16. **Kucuk, O**. Dietary Fat Reduction in Breast Cancer Prevention. Seminar, Tumor Board. Straub Medical Center, Honolulu, HI, January 10, 1994.

17. **Kucuk, O**. Biomarkers of Cancer Susceptibility. Seminar, Tumor Board. Straub Medical Center, Honolulu, HI, March 7, 1994.

18. **Kucuk, O**. Chemoprevention of Cancer. Seminar, Medical Staff Conference. Queen's Medical Center, Honolulu, HI, March 18, 1994.

19. **Kucuk, O**. Cancer Chemoprevention. Seminar, Tumor Board. Straub Medical Center, Honolulu, HI, May 9, 1994.

20. **Kucuk, O**. Dietary Interventions in Cancer Prevention. Seminar. Honolulu Medical Group, Honolulu, HI,

June 7, 1994.

21. **Kucuk, O**. Heritable Susceptibility to Cancer. Grand Rounds. Castle Medical Center, Kailua, HI, July 12, 1994.

22. **Kucuk, O**. Cancer Chemoprevention Prospects for 1997. Research Seminar. Cancer Research Center of Hawaii. University of Hawaii at Manoa, Honolulu, HI, March 31, 1997.

23. **Kucuk, O**. Current Status of Chemoprevention Research. Division of Hematology Oncology. University of Chicago. September 13, 1999.

24. **Kucuk, O**. Clinical Studies of Dietary Supplements and Herbal Products for Cancer Prevention. American College of Clinical Pharmacology 28th Annual Meeting and 1999 Frontiers Symposium. September 16-18, 1999. Doubletree Hotel, Rockville, MD.

25. **Kucuk, O.** "Occupational Cancer" in "Occupational Medicine: 2000 and Beyond". Annual Scientific Meeting of the Michigan Occupational and Environmental Medical Association. Ritz-Carlton Hotel, Dearborn, Michigan, September 24-25, 1999.

26. **Kucuk, O**. Preprostatectomy Model for Chemoprevention Studies. NIH workshop. Bethesda. August 7-9, 1999.

27. **Kucuk, O**. Oral Cancer Prevention by Fenretinide. Eighth Annual Oral Cancer Symposium. Sinai Hospital, Detroit, Michigan. Zuckerman Auditorium. March 17, 1999.

28. **Kucuk, O**. Chemoprevention and Nutrition in Cancer Prevention. KCI Conference for community oncologists and primary care physicians. Troy Marriott, Troy, MI, November 20, 1999.

29. **Kucuk, O**. Soy Isoflavones and Carotenoids in Prevention of Prostate Cancer. University of Texas Southwestern Medical School, Division of Medical Oncology, Simmons Cancer Center, Dallas, TX. November 8, 1999.

30. **Kucuk, O**. Lycopene in Cancer Prevention. Antioxidants' New Colors: Newspaper and magazine editors' conference. New York, NY, November 16, 1999.

31. **Kucuk, O**. Lycopene in Preprostatectomy Patients. NIH Workshop on Prostate Cancer Chemoprevention. August 7-9, 1999, Baltimore, MD.

32. **Kucuk, O**. Preneoplasia and Chemoprevention of Head and Neck Cancer. SWOG Clinical Research Associates Committee Continuing Education Workshop on Head and Neck Cancer. October 21, 1999, San Diego, California.

33. **Kucuk, O**. Invited Lecture: Lycopene in Prostate Cancer Prevention. University of Pittsburgh Cancer Institute Prostate Research group presentation. Pittsburgh, PA. March 24, 2000.

34. **Kucuk, O**. Invited lecture: "Lycopene and soy isoflavones in cancer prevention". Michigan State University, Department of Human Nutrition and Food Sciences. East Lansing, Michigan. March 29, 2000.

35. **Kucuk, O**. Invited lecture: "Lycopene and soy isoflavones in prostate cancer prevention". Midwest Regional Chapter, Society of Toxicology, 2000 Annual Spring Meeting. "From Mouse to Human: Breast, Ovarian and Prostate Cancer". Marriott Lincolnshire Resort, Lincolnshire, Illinois, May 12, 2000.

36. **Kucuk, O**. Invited Lecture: "Oral Preneoplasia: Strategies for Cancer Prevention". Ninth Annual Oral Cancer Symposium. University of Detroit Mercy School of Dentistry. Ward Conference Center. 5200 W.

Outerdrive, Detroit, MI. May 17, 2000.

37. **Kucuk, O**. Lycopene in Prostate Cancer Prevention. Memorial Seminar for Professor Rafael (Rafi) Frankel. Cohen Auditorium, Volcani Center, Department of Agriculture, Beit Dagan, Tel Aviv, Israel, January 26, 2000.

38. **Kucuk, O**. Carotenoids and Isoflavones in Prostate Cancer Prevention. Department of Oncology, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel, January 27, 2000.

39. **Kucuk, O**. "Interactions between CAM Therapy and Chemotherapy in Oncology". Virginia Hematology and Oncology Society. McLean, Virginia. October 27, 2001.

40. **Kucuk, O**. "CAM Therapy in Oncology." Nevada Oncology Society. Reno, Nevada. November 10, 2001.

41. **Kucuk, O**. Carotenoids and isoflavones in prostate cancer prevention. Oral presentation at Proutsneck Prostate Cancer Meeting (Robert Getzenberg & Kenneth Pienta, organizers): 11/09/02

42. **Kucuk, O**. Moffitt Cancer Center Grand Rounds: Soy and lycopene in cancer prevention. Tampa, FL. 4/30/03

43. **Kucuk, O.** Ohio State University, Cancer Prevention Program Research Seminar: Soy and Lycopene in Prostate Cancer. Columbus, Ohio. 11/3/03

44. **Kucuk, O.** "Nutrition in Cancer Prevention and Treatment". Children's Hospital of Michigan, Hematology/Oncology Division, Detroit, Michigan. 2/23/04

45. **Kucuk, O**. "New Developments in Head and Neck Cancer Treatment". Flower Hospital Oncology Department, Toledo, OH. 3/24/04

46. **Kucuk, O**. Advances in the Treatment of Head and Neck Cancer. ProMedica Health System. Flower Hospital, Toledo, OH. 01/18/06

47. **Kucuk, O**. Meharry Medical College, Department of Surgery, Prostate Cancer Research Program Seminar Series: March 5, 2007.

48. **Kucuk, O.** Title: lycopene in the etiology and control of prostate cancer progression, Nashville, TN. March 5, 2007

49. **Kucuk, O**. MEDICAL GRAND ROUNDS: Title: advances in head and neck cancer treatment. Northern Michigan Hospital, Petoskey, MI. May 16, 2007

50. **Kucuk, O.** Hematology/Oncology Grand Rounds, University of Miami, Miami, FL. Title: New advances in head and neck cancer therapy. November 14, 2007

51. **Kucuk, O**. Emory University School of Medicine, Department of Medicine Grand Rounds. Title: Nutrition in Prevention and Treatment of Prostate Cancer October 28, 2008

Presentations at Wayne State University/ Karmanos Cancer Institute

52. **Kucuk, O**. Cholesterol Oxides and Cancer. Multidisciplinary Lung Program Research Seminar. Wertz Clinical Cancer Center, Harper Hospital, Detroit, MI, June 1, 1995.

53. **Kucuk, O**. Cholesterol Oxides and Cancer. Seminar. Epidemiology Program, Michigan Cancer Foundation, Detroit, MI, July 26, 1995.

54. **Kucuk, O**. Cholesterol Oxides and Cancer. Research Seminar, NFS 785 Graduate Seminars. Department of Nutrition and Food Science, Wayne State University, Science Hall, Detroit, MI, September 26, 1995.

55. **Kucuk, O**. Cholesterol Oxides and Cancer. Grand Rounds. Division of Hematology and Oncology, WSU, Harper Hospital; Detroit, MI, October 11, 1995.

56. **Kucuk, O.** Cholesterol Oxidation and Cancer. Research Seminar. Department of Internal Medicine, Wayne State University School of Medicine, Harper Hospital, Detroit, MI, November 17, 1995.

57. **Kucuk, O**. Cholesterol Oxides and Cancer. Research Seminar. Institute of Chemical Toxicology, Wayne State University, Detroit, MI, January18, 1996.

58. **Kucuk, O**. Cancer Prevention: Chemoprevention and Nutritional Intervention Controversies. Grand Rounds. Department of Internal Medicine, Wayne State University. March 13, 1996.

59. **Kucuk, O**. Mutagen Sensitivity and Plasma Micronutrients. HAC (Human Applications) Research Seminar. Institute of Chemical Toxicology, Wayne State University, Detroit, MI, May 14, 1996.

60. **Kucuk, O**. Mutagen Sensitivity and Micronutrients. Cancer Prevention Task Force Research Seminar. Karmanos Cancer Institute, Detroit, MI, June 7, 1996.

61. **Kucuk, O.** Prevention of Prostate Cancer by Lycopene. Urologic Oncology Conference. Karmanos Cancer Institute, Detroit, MI, May 21, 1997.

62. **Kucuk, O.** Prevention of Breast Cancer by Soy Isoflavones. Breast Cancer Multidisciplinary Conference, Karmanos Cancer Institute; September 9, 1998.

63. **Kucuk, O.** Breast Cancer Prevention Program. Breast Cancer Program Retreat. Karmanos Cancer Institute. September 18, 1998.

64. **Kucuk, O.** Chemoprevention of Prostate Cancer with Lycopene. Department of Urology, Karmanos Cancer Institute, December 16, 1998.

65. **Kucuk, O**. Cancer Chemoprevention. Grand Rounds, Division of Hematology and Oncology, Karmanos Cancer Institute. January 4, 1999.

66. **Kucuk, O**. Prostate Cancer Chemoprevention with Lycopene and Soy Isoflavones. James M. Pierce, Jr., M.D. Memorial Lecture and Prostate Cancer Symposium. Karmanos Cancer Institute, Wertz Clinical Cancer Center, Second Floor Auditorium. April 9, 1999.

67. **Kucuk, O.** Soy Isoflavones in Breast Cancer Chemoprevention. Breast Cancer Program Retreat, Karmanos Cancer Institute, September 10, 1999.

68. **Kucuk, O.** Soy Isoflavones in Breast Cancer Chemoprevention. Breast Cancer Program Weekly Conference, Karmanos Cancer Institute. October 25, 1999.

69. **Kucuk, O.** Soy Isoflavones in Prostate Cancer Chemoprevention. Urologic Oncology Program Weekly Conference, Karmanos Cancer Institute. October 27, 1999.

70. **Kucuk, O.** Interactions Between Tobacco and Nutrition. Symposium: Biological and Behavioral Aspects of Nicotine Use Research Conference. WSU Smoking and Illness Interdisciplinary Research Initiative (Steering Committee: Ada Jacox, Diane Brown, Gloria Heppner, Virginia Rice, Leslie Schuh). November 18, 1999.

71. **Kucuk, O.** "Soy Isoflavones and Lycopene in Cancer Prevention". Department of Nutrition and Food Science, Wayne State University. November 28, 2000.

72. **Kucuk, O.** "Management of Metastatic Head and Neck Cancer". Department of Otolaryngology Grand Rounds. February 7, 2001. Harper Hospital, 4 Morse Auditorium.

73. **Kucuk, O.** "New Strategies in Cancer Prevention". WSU Department of Internal Medicine Grand Rounds. March 7, 2001. Scott Hall, Blue Auditorium.

74. **Kucuk, O.** "Chemoprevention of Lung Cancer". Lung Service Weekly Conference, Karmanos Cancer Institute. May 10, 2001.

75. **Kucuk, O.** "Cancer Prevention". WSU Department of Internal Medicine Grand Rounds. March 12, 2003. Scott Hall, Blue Auditorium.

76. **Kucuk, O.** "Cancer Prevention". Sinai Grace Hospital, Department of Medicine Grand Rounds. December 18, 2003.

77. **Kucuk, O.** IEHS Seminar Series: Title of the presentation: Soy isoflavones in cancer prevention and treatment. Institute of Environmental Health Sciences, WSU, Detroit, MI. October 19, 2006

78. **Kucuk, O.** Department of Otolaryngology and Head and Neck Surgery Grand Rounds Title: CHEMOPREVENTION OF HEAD AND NECK CANCER, Wayne State University, Karmanos Cancer Institute, Detroit. May 30, 2007

INVITATIONS TO NATIONAL OR INTERNATIONAL CONFERENCES

INTERNATIONAL

1. **Küçük, Ö.**, Kauffman, J.W. Free Radicals, Oxygen and Radiation. International Seminar on the Living System, New Delhi, India, 1983. (slide presentation by Prof. Kauffman)

2. Kies, M.N., Vriesendorp, H.M., Gordon, L.I., **Küçük, Ö.**, Rosen, S.T., Fey, T.A., McDonough, C., Prachand, S. Autologous Bone Marrow Transplantation in Metastatic Breast Cancer. International Society of Experimental Hematology Meeting, 1983.

3. Rooney, M.W., Kauffman, J.W., **Küçük, Ö.**, Kwaan, H.C. Red Blood Cell Hyperaggregability Due to Increased Protein Alpha-helical Order of Fibrinogen in Patients with Distal Extremity Gangrene. International Society of Thrombosis and Haemostasis Meeting, 1985.

4. Lis, L.J., **Küçük, Ö.**, Westerman, M.P., Cunningham, B.A., Wolfe, D.H., Collins, J.M., Quinn, P.J., Tamura-Lis, W. The influence of oxidized sterol compounds on phase transitions in lipid model membrane systems. International Biophysics Congress, Vancouver, BC, Canada, 1990.

5. **Küçük, Ö.**, Lis, L.J., Westerman, M.P., Cunningham, B.A., Collins, J.M., Quinn, P.J., Wolfe, D.H., Tamura-Lis, W. The influence of oxidized sterol compounds on the phase structures and transitions in lipid model membrane systems. International Liquid Crystal Meeting, Vancouver, BC, Canada, 1990.

6. Collins, J.M., Cunningham, B.A., **Küçük, Ö.**, Westerman, M.P., Lis, L.J. The influence of thermochemical fluctuation forces on interaction between neutral and charged phospholipid bilayers. International Liquid Crystal Meeting, Vancouver, BC, Canada, 1990.

7. Cunningham, B.A., Quinn, P.J., Collins, J.M., **Küçük, Ö.**, Westerman, M.P., Lis, L.J. Phase transition

mechanisms involving interdigitated lipid bilayers. International Liquid Crystal Meeting, Vancouver, BC, Canada, 1990.

8. **Küçük, Ö.**, Lis, L.J., Dey, T., Mata, R., Westerman, M.P., Chamberlain, B., Gage, D., Sweeley, C., Quinn, P.J., Szostek, R., Kauffman, J.W., Yachnin, S. Oxidized sterol compounds are present and modify the lipid bilayer in sickle red blood cell membranes. International Biophysics Congress, Vancouver, BC, Canada, 1990.

9. **Kucuk, O.** Chemoprevention of Cancer. Sixteenth Annual FHP International Medical Symposium. Guam. October 27-30, 1993.(slide presentation)

10. **Kucuk, O.** Dietary Interventions in Cancer Prevention. Sixteenth Annual FHP International Symposium. Guam. October 27-30, 1993.(slide presentation)

11. **Kucuk, O**. Cholesterol Oxides and Cancer. International Congress on Free Radicals in Health and Disease. Istanbul, Turkey. September 6-10, 1995.(slide presentation)

12. **Kucuk O,** Sarkar F, Sakr W, Djuric Z, Velazquez F, Wood D, Crissman J, Bertram J. Lycopene decreases serum PSA and tumor volume in PCa. International Conference on Diet and Cancer Prevention. Tampere, Finland, June 15,1999. (poster presentation)

13. **Kucuk O**, Sakr W, Sarkar F, Djuric Z, Velazquez F, Khachik F, Pollack M, Crissman J, Pontes E, Bertram J, Wood DP. Effects of lycopene on prostatic tissue biomarkers, PSA levels, clinicopathologic parameters, lycopene metabolites, and serum IGF-1/IGFBP-3 levels. International Carotenoid Meeting, Cairns, Australia, July 21, 1999. (oral presentation).

14. **Kucuk, O.** Nutrition in Prostate Cancer Prevention International Symposium. Toronto, Ontario, Canada. March 3-4, 2000. Two talks (1) Lycopene in prostate cancer prevention, clinical data. (2) Study design for prostate cancer prevention clinical trials.

15. **Kucuk, O.** Millennium International Urology Conference. Invited plenary session speaker: "Lycopene in Prostate Cancer Prevention". New Delhi, India. November 1, 2000.

16. **Kucuk, O.** "Lycopene in Prostate Cancer Prevention". Department of Experimental Pathology and Therapeutics, National Cancer Center, Tsukiji, Tokyo, Japan. October 30, 2000.

17. **Kucuk, O**. "Lycopene in Prostate Cancer Chemoprevention". Department of Medical Oncology. Johns Hopkins Singapore Unit and National University of Singapore. November 1, 2000.

18. **Kucuk, O.** "Lycopene in Prostate Cancer Prevention". Memorial Seminar for Professor Rafael (Rafi) Frankel. Department of Agriculture, Beit Dagan, Tel Aviv, Israel, January 26, 2000.

19. **Kucuk, O.** "Carotenoids and Isoflavones in Prostate Cancer Prevention". Department of Oncology, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel, January 27, 2000.

20. **Kucuk, O.** "Lycopene in prostate cancer prevention, clinical data". Nutrition in Prostate Cancer Prevention International Symposium. Toronto, Ontario, Canada. March 3-4, 2000.

21. **Kucuk, O.** "Study design considerations for prostate cancer prevention clinical trials". Nutrition in Prostate Cancer Prevention International Symposium. Toronto, Ontario, Canada. March 3-4, 2000.

22. **Kucuk, O.** Modulation of Prostate Cancer Growth and Differentiation by Lycopene. UICC International Prostate Cancer Meeting. Eilat, Israel, 1/23-1/25, 2000.

23. **Kucuk, O.** Modulation of IGF-1 and IGFBP-3 by Lycopene in Prostate CancerUICC International Prostate Cancer Meeting. Eilat, Israel, 1/23-1/25, 2000.

24. **Kucuk, O.** "Lycopene in Prostate Cancer Prevention". Millennium International Urology Congress. Invited speaker. New Delhi, India. November 1, 2000.

25. **Kucuk, O.** "Prevention of Oral cancer: Treatment of Premalignant Lesions with Chemopreventive Agents: Soy, Lycopene and Retinoids". American Association of Oral and Maxillofacial Surgery Annual Meeting. San Francisco. September 22, 2000.

26. **Kucuk, O.** "Lycopene Clinical Trial in Localized Prostate Cancer". International Symposium on the Role of Tomato Products and Carotenoids in Disease Prevention. The New York Academy of Medicine. New York City, NY. April 10-11, 2001. Sponsored by American Health Foundation.

27. **Kucuk, O.** "Soy isoflavones in the treatment of prostate cancer". Presentation at Fourth International Symposium on the Role of Soy in Preventing and Treating Chronic Disease. San Diego, CA, November 4-7, 2001.

28. **Kucuk, O.** "Soy isoflavones in the treatment of prostate cancer". Presentation at AACR Special Conference, Co-chairs: K. Pienta, R. Getzenberg & D. Coffey: New Discoveries in Prostate Cancer Biology and Treatment". Naples, FL. December 5-9, 2001.

29. **Kucuk, O.** Lycopene in Prostate Cancer Prevention". Department of Urology, Celal Bayar University, Manisa, Turkey, June 19, 2001.

30. **Kucuk, O.** Lycopene in prostate cancer prevention. Urology Department, Akdeniz University, Antalya, Turkey. June 15, 2001

31. **Kucuk, O.** "Lycopene in Prostate Cancer Prevention". Thirteenth International Carotenoid Conference, Honolulu, Hawaii, January 6-12, 2002.

32. **Kucuk, O.** "Carotenoids and isoflavones in prostate cancer prevention" Proutsneck Prostate Cancer Meeting (Getzenberg & Pienta): 11/9/02

33. **Kucuk, O.** Lectures at University of Sao Paolo (Sao Paolo), Cancer Center (Fortaleza) and Medical Oncology Society Meeting (Curitiba) in Brazil. Program organized by Dr. Edson Pontes, Asst Dean for International Programs, WSU. (3/19/03 – 3/26/03)

34. **Kucuk, O.** Presentation at the Global Soy Conference, Fos do Iguassu, Brazil. Title: Soy Isoflavones in Cancer Prevention and Treatment. 3/1/04 - 3/5/04

35. **Kucuk, O.** Six Lectures at University of UNESP Botucatu (Botucatu), Cancer Center of Ceara (Fortaleza) and Medical Oncology Society Meeting Curitiba) in Brazil. Program organized by Dr. Edson Pontes, Asst Dean for International Programs, WSU. 3/7/04 - 3/13/04

36. **Kucuk, O.** Four Lectures at University of Ankara (Ankara), and Akdeniz University (Antalya) in Turkey. Program organized by Dr. Edson Pontes, Asst Dean for International Programs, WSU and Dr. Omer Kucuk. 9/27/04 - 10/1/04

37. **Kucuk, O.** Presentations and Session Chairman (Nutrition and Cancer Prevention) at the International Society of Preventive Oncology (ISPO), Nice, France. Titles: (1) Soy in cancer prevention. (2) Lycopene in prostate cancer prevention. 2/7/04 - 2/11/04

38. **Kucuk, O.** World Soy Foods Summit, San Diego, CA. Soy in cancer prevention and treatment. 2/18/04 - 2/19/04

39. **Kucuk, O.** Turkish Head and Neck Cancer Society Annual Meeting. New developments in the treatment of nasopharyngeal cancer. 9/25/04 - 9/27/04

40. **Kucuk, O.** Turkish Society of Hematology Annual Meeting. Title: Soy isoflavones enhance efficacy of CHOP chemotherapy in an animal model. 9/23/04 - 9/25/04

41. **Kucuk, O.** Otolaryngology Meeting, Ankara, Turkey. Lecture on "Soy isoflavones in head and neck cancer prevention and treatment". 4/1/05-4/4/05

42. Karp D, Lee S, Keller S, Johnson D, **Kucuk O**, Clamon G, Marks R, Johnston M, Okawara G, Ruckdeschel J. Interim Report: A Phase III Randomized Double Blind Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non Small Cell Lung Cancer. Lung Cancer 49 (supplement 2): S181 (P-252), 2005. Poster presentation at IASLC, July, 2005, Barcelona, Spain.

43. **Kucuk, O.** Four Lectures on "Lung Cancer Prevention and Treatment" at University of Ankara (Ankara), Hacettepe University (Ankara), Florence Nightingale Metropolitan Cancer Center (Istanbul) and Akdeniz University Antalya) in Turkey. Program organized by Dr. Edson Pontes, Asst Dean for International Programs, WSU and Dr. Omer Kucuk. 11/9/05 - 11/16/05

44. Four lectures on "Nutrition and Cancer Prevention" and Nutrition and Cancer Therapy" in Curitiba and Fortaleza, Brazil. Symposium title: Cancer Risk Assessment, Prevention and Early Detection. Organized by **Dr. Omer Kucuk** and Dr. Edson Pontes, Asst Dean for International Programs, WSU. 3/14/06-3/18/06

45. **Kucuk, O.** Two lectures on "Cognitive effects of cancer therapy" and "Prevention of Cancer Treatment Toxicities by Soy Isoflavones" at Bakirkoy Days: International Meeting of Neurosurgery and Behavioral Disorders. Istanbul, Turkey. 05/08/06-05/11/06

46. Three lectures on "New Developments in Cancer Chemoprevention" at symposia entitled New Developments in Oncology at University of Ankara (Ankara), Florence Nightingale Metropolitan Cancer Center (Istanbul) and Akdeniz University (Antalya) in Turkey. Programs were organized by **Dr. Omer Kucuk** and Dr. Edson Pontes, Asst Dean for International Programs, WSU. 10/30/06 - 11/03/06

47. **Kucuk, O.** Curitiba, Salvador and Fortaleza, Brazil: Cancer symposia: New developments in cancer therapy.Title: Intra-operative and intra-arterial chemotherapy. (Same talk in three cities). 3/17-3/26/07

48. **Kucuk, O.** National Cancer Congress, Antalya, TURKEY; Two oral presentations: 4/23/07 New Developments in Lung Cancer Chemoprevention. 4/22/07 Meet the expert: Chemoprevention.

49. **Kucuk, O.** FIRST ANNUAL USA-QATAR INTERNATIONAL CANCER SYMPOSIUM: STATE OF THE ART ; THERAPY OF ADULT AND CHILDHOOD CANCERS; Oral presentation: Targeted therapy for renal cancer; Moderator: Session on "Genitourinary cancers". Doha, Qatar, April 29 to May 1, 2007

50. Yildirim-Kupesiz G, Sakr W, Cher M, Banerjee M, Pontes E, Parnes H, **Kucuk O**. Effect of soy isoflavone supplementation on prostate tissue, markers of proliferation and apoptosis, and histopathological endpoint of tumor grade, volume and stage. September 8-13, 2007. 21st European Congress of Pathology.(www.ecp2007istanbul.org). Poster presentation.

51. **Kucuk, O.** Fortaleza National Breast Cancer Meeting. Oral presentation: Breast cancer chemoprevention. 10/18-10/25/07

52. **Kucuk O**, Pass H, Lonardo F, Gazdar A, Madan S, Abrams J, Maddipati KR, Upfal M, Soubani A, Honn

KV, Szabo E. Phase II clinical trial of zileuton in persons with bronchial dysplasia. AACR Frontiers in Cancer Prevention Meeting, Philadelphia, December 5-8, 2007. Poster presentation.

53. **Kucuk, O.** First International Congress on Nutrition and Cancer) in Antalya, Turkey (www.nutritioncancer2008.org) "Lycopene and soy isoflavones in prostate cancer" and chaired a session at the meeting. Also on organizing committee. May 19-23 2008

54. **Kucuk, O.** "Lycopene and soy isoflavones in prostate cancer treatment". Oral presentation at International Carotenoid Conference. Okinawa, Japan, June 26, 2008.

55. **Kucuk, O.** First International Cancer Prevention Symposium, Izmir, Turkey, "Lycopene and soy in cancer prevention" September 13-16, 2008.

56. **Kucuk, O.** "Soy isoflavones as an adjunct to radiation in prostate cancer treatment". Oral presentation at the Eighth International Conference on the role of Soy in Prevention and Treatment of Chronic Disease. Tokyo, Japan. November 8-12, 2008.

57. **Kucuk, O.** "Modulation of biomarkers of growth and differentiation in breast cancer by soy isoflavones". Oral presentation at the Eighth International Conference on the role of Soy in Prevention and Treatment of Chronic Disease. Tokyo, Japan. November 8-12, 2008.

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35. **Kucuk, O.** Gemzar and Taxol Combination in the Treatment of Advanced Head and Neck Cancer. The Fox Chase Cancer Center Investigators Workshop. March 3-6, 1999, Lanai, Hawaii.

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38. **Kucuk, O.** Annual Meeting of American Association of Oral and Maxillofacial Surgery. San Francisco. September 22, 2000. Prevention of Oral cancer: Treatment of Premalignant Lesions with Chemopreventive Agents: Soy, Lycopene and Retinoids.

39. **Kucuk, O** "Soy and hormone receptors: To use or not to use?". Annual NOAT Conference. September 7-9, 2000. Philadelphia, PA.

40. **Kucuk, O** "Research Opportunities in Nutritional Oncology". Annual NOAT Conference. September 7-9, 2000. Philadelphia, PA.

41. **Kucuk, O** Department of Defense Era of Hope Meeting on Breast Cancer. "Modulation of cell growth and differentiation and oxidative stress by soy isoflavones in breast cancer patients". June 8-12, Atlanta, Georgia. 2000

42. **Kucuk, O** Treatment of Head and Neck Cancer. Oral presentation at Michigan Pharmacists Association 2003 Annual Convention and Exposition:. 2/22/2003

43. **Kucuk, O** Lycopene in prostate cancer prevention. Oral presentation at Annual CERES conference. University of Virginia. Washington DC. 4/1/2003

44. **Kucuk, O** Lung cancer prevention and treatment: role of pathology and biomarker studies. Oral presentation at SWOG Nursing Oncology Committee Plenary Session. 4/11/2003

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49. **Kucuk, O** Session Chairman and Organizer (Soy and Cancer Therapy) at the Annual Meeting of American College of Nutrition. 9/22/05 - 9/25/05

50. Raffoul JJ, Wang Y, **Kucuk O,** Sarkar FH, Hillman GG. Molecular Mechanism Involved in Enhanced Cell Killing by Genistein and Radiation in Prostate Cancer Cells. AACR, April 16-20, 2005.

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Persons with Resected Stage I Non Small Cell Lung Cancer. A Year-Six Update. AACR Annual Cancer Prevention Meeting November 12-15, 2006. Poster Presentation

53. **Kucuk, O.** Two presentations at an NIH meeting: "Soy Isoflavones in Cancer Prevention" and "Zileuton in Lung Cancer Prevention" at the NIH Annual Summer SPORE workshop, July 2006. 07/17/06-07/19/06

54. **Kucuk, O.** NCI Lung and Head/Neck SPORE Meeting, Charleston, SC. TITLE: SOY ISOFLAVONES IN AERODIGESTIVE CANCER PREVENTION. 2/7/07

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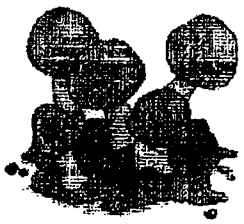

Scientific Name

Agaricus blazei Murrill

TOP

Common Name

Himematsutake, Agarikusutake, Kawarihiratake, Cogumelo do Sol, Sun mushroom

TOP

Clinical Summary

Agaricus blazei is an edible mushroom native to Brazil and cultivated in Japan for its medicinal uses. It has been used to treat arteriosclerosis, hepatitis, hyperlipidemia, diabetes, dermatitis, and cancer. In vitro experiments and studies done in mice have shown that Agaricus has immunomodulatory, antitumor, and antimutagenic properties. The polysaccharides and anti-angiogenic compounds present in Agaricus are thought to be responsible for its antitumor properties. Such effects are believed to be exerted by immunopotentiation or direct inhibition of angiogenesis (1) (2) (3) (4) (5) (6). A recent randomized study showed that oral administration of Agaricus extract improved the natural killer cell

activity and quality of life in gynecological cancer patients undergoing chemotherapy [7]. However, more studies are needed to confirm these observations. Agaricus was also shown to have antidiabetic effects in vitro and in animal studies [10] [11]. In addition, results from a study done in human subjects with type 2 diabetes suggest benefits of agaricus extract in improving insulin resistance [13]. Liver damage and deaths following consumption of Agaricus have been reported [12]. Due to its immunopotentiating effects, Agaricus can potentially interfere with immunomodulating drugs althought such interactions have not been studied.

TOP

Food Sources

Agaricus is an edible fungus. It is available as freeze-dried mushroom or as concentrated liquid extracts, teas, or capsules. The whole mushroom is often added to soups, sauces, or hot teas.

TOP

Purported uses

- Arteriosclerosis
- Cancer treatment
- Diabetes
- Hepatitis
- Hyperlipidemia
- Stimulant

TOP

Constituents

- Polysaccharides: β-1, 6-D-glucan
- Sterols: Ergosterol
- Linoleic acid
- Lipids
- Anti-angiogenic compounds: Sodium pyroglutamate (A-1) and A-2 [1] [2]

TOP

Mechanism of Action

A major constituent of Agaricus, ergosterol, was found to inhibit tumor growth in mice via direct inhibition of tumor-induced angiogenesis [2]. Other studies demonstrated that polysaccharides present in Agaricus extract caused activation of macrophages [6] or natural killer cells [8] and induced cytotoxic T-lymphocyte activity in tumor-bearing mice. Both aqueous and organic extracts of Agaricus offered protection to cells exposed to methyl methanesulphonate, a mutagenic agent. The stimulus produced by linoleic acid on β DNA polymerase, an enzyme involved in repair mechanism following exposure of DNA to alkylating agents, is thought responsible for such an effect [2].

TOP

Contraindications

Hypersensitivity to Agaricus.

TOP

Adverse Reactions

Consumption of Agaricus has been associated with hepatic dysfunction in cancer patients (12).

TOP

Herb-Drug Interactions

Because Agaricus extract activates the immune system, it may interfere with certain drugs that modulate the immune system.

TOP

Lab Interactions

- May lower blood glucose level (10).
- May cause elevation of liver enzymes (12).

TOP

Literature Summary and Critique

Ahn W.-S, et al. Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, Agaricus blazei Murrill Kyowa, in gynecological cancer patients undergoing chemotherapy. *Int J Gynecol Cancer* 2004; 14:589-594.

In this study 100 patients with cervical, ovarian, and endometrial cancers were treated with either carboplatin plus VP16 (etoposide), or carboplatin plus taxol every three weeks for at least three cycles. They were randomized to receive oral Agaricus extract (three packs per day, one pack each time) or placebo along with the treatments. Blood samples were drawn one day before first chemotherapy and one day before second chemotherapy. Researchers found that the Agaricus group had a significantly higher natural killer cell activity compared to those on placebo. In addition there was improvement in chemotherapy associated side effects such as emotional instability, alopecia, general weakness, and decrease in appetite. However, there was no difference in lymphokine-activated killer and monocyte activities between the two groups. Further studies are required to confirm these observations.

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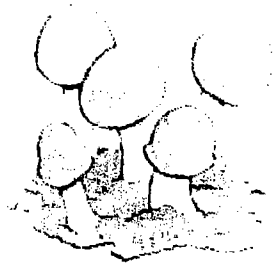

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Scientific Name

Agaricus blazei Murrill

Common Name

Himematsutake, Agarikusutake, Kawarihiratake, Cogumelo do Sol, Sun mushroom

Clinical Summary

Agaricus blazei is an edible mushroom native to Brazil and cultivated in Japan for its medicinal uses. It has been used to treat arteriosclerosis, hepatitis, hyperlipidemia, diabetes, dermatitis, and cancer. In vitro experiments and studies done in mice have shown that Agaricus has immunomodulatory, antitumor, and antimutagenic properties. The polysaccharides and anti-angiogenic compounds present in Agaricus are thought to be responsible for its antitumor properties. Such effects are believed to be exerted by immunopotentiation or direct inhibition of angiogenesis [1] [2] [3] [4] [5] [6]. A recent randomized study showed that oral administration of Agaricus extract improved the natural killer cell activity and quality of life in gynecological cancer patients undergoing chemotherapy [7]. However, more studies are needed to confirm these observations. Agaricus was also shown to have antidiabetic effects in vitro and in animal studies [10] [11]. In addition, results from a study done in human subjects with type 2 diabetes suggest benefits of agaricus extract in improving insulin resistance [13]. Liver damage and deaths following consumption of Agaricus have been reported [14]. Due to its immunopotentiating effects, Agaricus can potentially interfere with immunomodulating drugs althought such interactions have not been studied.

Food Sources

Agaricus is an edible fungus. It is available as freeze-dried mushroom or

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as concentrated liquid extracts, teas, or capsules. The whole mushroom is often added to soups, sauces, or hot teas.

TOP

Purported uses

- Arteriosclerosis
- Cancer treatment
- Diabetes
- Hepatitis
- Hyperlipidemia
- Stimulant

TOP

Constituents

- Polysaccharides: β-1, 6-D-glucan
- Sterols: Ergosterol
- Linoleic acid
- Lipids
- Anti-angiogenic compounds: Sodium pyroglutamate (A-1) and A-2 (1) (2)

TOP

Mechanism of Action

A major constituent of Agaricus, ergosterol, was found to inhibit tumor growth in mice via direct inhibition of tumor-induced angiogenesis (1). Other studies demonstrated that polysaccharides present in Agaricus extract caused activation of macrophages (6) or natural killer cells (9) and induced cytotoxic T-lymphocyte activity in tumor-bearing mice. Both aqueous and organic extracts of Agaricus offered protection to cells exposed to methyl methanesulphonate, a mutagenic agent. The stimulus produced by linoleic acid on β DNA polymerase, an enzyme involved in repair mechanism following exposure of DNA to alkylating agents, is thought responsible for such an effect (9).

TOP

Contraindications

Hypersensitivity to Agaricus.

Adverse Reactions

Consumption of Agaricus has been associated with hepatic dysfunction in cancer patients [13].

Herb Drug Interactions

Because Agaricus extract activates the immune system, it may interfere with certain drugs that modulate the immune system.

Lab Interactions

- May lower blood glucose level [19].
- May cause elevation of liver enzymes [13].

Literature Summary and Critique

Ahn W.S, et al. Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, Agaricus blazei Murrill Kyowa, in gynecological cancer patients undergoing chemotherapy. Int J Gynecol Cancer 2004; 14:589-594.

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samples were drawn one day before first chemotherapy and one day before second chemotherapy. Researchers found that the Agaricus group had a significantly higher natural killer cell activity compared to those on placebo. In addition there was improvement in chemotherapy associated side effects such as emotional instability, alopecia, general weakness, and decrease in appetite. However, there was no difference in lymphokine-activated killer and monocyte activities between the two groups. Further studies are required to confirm these observations.

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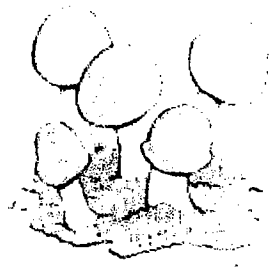

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Scientific Name

Agaricus blazei Murrill

Common Name

Himematsutake, Agarikusutake, Kawarihiratake, Cogumelo do Sol, Sun mushroom

Clinical Summary

Agaricus blazei is an edible mushroom native to Brazil and cultivated in Japan for its medicinal uses. It has been used to treat arteriosclerosis, hepatitis, hyperlipidemia, diabetes, dermatitis, and cancer. In vitro experiments and studies done in mice have shown that Agaricus has immunomodulatory, antitumor, and antimutagenic properties. The polysaccharides and anti-angiogenic compounds present in Agaricus are thought to be responsible for its antitumor properties. Such effects are believed to be exerted by immunopotentiation or direct inhibition of angiogenesis [1] [2] [3] [4] [5] [6]. A recent randomized study showed that oral administration of Agaricus extract improved the natural killer cell activity and quality of life in gynecological cancer patients undergoing chemotherapy [7]. However, more studies are needed to confirm these observations. Agaricus was also shown to have antidiabetic effects in vitro and in animal studies [10] [11]. In addition, results from a study done in human subjects with type 2 diabetes suggest benefits of agaricus extract in improving insulin resistance [13]. Liver damage and deaths following consumption of Agaricus have been reported [12]. Due to its immunopotentiating effects, Agaricus can potentially interfere with immunomodulating drugs althought such interactions have not been studied.

Food Sources

Agaricus is an edible fungus. It is available as freeze-dried mushroom or

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as concentrated liquid extracts, teas, or capsules. The whole mushroom is often added to soups, sauces, or hot teas.

Purported uses

- Arteriosclerosis
- Cancer treatment
- Diabetes
- Hepatitis
- Hyperlipidemia
- Stimulant

00047

Constituents

- Polysaccharides: β-1, 6-D-glucan
- Sterols: Ergosterol
- Linoleic acid
- Lipids
- Anti-angiogenic compounds: Sodium pyroglutamate (A-1) and A-2 (1) (2)

Mechanism of Action

A major constituent of Agaricus, ergosterol, was found to inhibit tumor growth in mice via direct inhibition of tumor-induced anglogenesis (4). Other studies demonstrated that polysaccharides present in Agaricus extract caused activation of macrophages (6) or natural killer cells (8) and induced cytotoxic T-lymphocyte activity in tumor-bearing mice. Both aqueous and organic extracts of Agaricus offered protection to cells exposed to methyl methanesulphonate, a mutagenic agent. The stimulus produced by linoleic acid on β DNA polymerase, an enzyme involved in repair mechanism following exposure of DNA to alkylating agents, is thought responsible for such an effect (9).

Contraindications

Hypersensitivity to Agaricus.

Adverse Reactions

Consumption of Agaricus has been associated with hepatic dysfunction in cancer patients [12].

Herb-Drug Interactions

Because Agaricus extract activates the immune system, it may interfere with certain drugs that modulate the immune system.

Lab Interactions

- May lower blood glucose level [10].
- May cause elevation of liver enzymes [12].

Literature Summary and Critique

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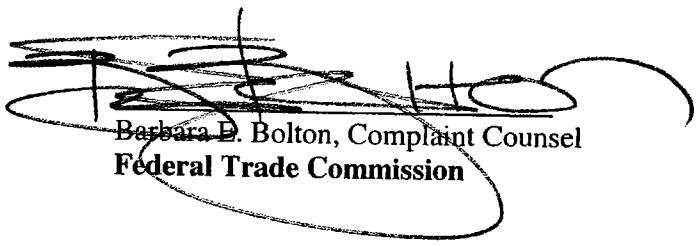

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Original Article

Immunomodulating Activity of *Agaricus brasiliensis* KA21 in Mice and in Human Volunteers

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We performed studies on murine models and human volunteers to examine the immunoenhancing effects of the naturally outdoor-cultivated fruit body of *Agaricus brasiliensis* KA21 (i.e. *Agaricus blazei*). Antitumor, leukocyte-enhancing, hepatopathy-alleviating and endotoxin shock-alleviating effects were found in mice. In the human study, percentage body fat, percentage visceral fat, blood cholesterol level and blood glucose level were decreased, and natural killer cell activity was increased. Taken together, the results strongly suggest that the *A. brasiliensis* fruit body is useful as a health-promoting food.

Keywords: *A. brasiliensis* – clinical research – cold water extract – NK activity – outdoor-cultivated – safety

Alternative medicine is the general term for 'medicine and treatment that have not been verified scientifically or applied clinically in modern Western medicine' (1–12). The range of alternative medicine varies widely to include traditional medicine and folk remedies as well as new therapies that are not covered by health insurance. Considering the current world population, the percentage of people utilizing modern Western medicine is surprisingly low, with the World Health Organization (WHO) indicating that 65–80% of health management is by traditional medicine. 'Mibyou' is a recently established term that means a half-sick person having clinical laboratory data that borders healthy individuals and patients. Education of the mibyou population about eating habits is also significantly important for maintaining public health by the government.

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In Japan, an increasing number of people are turning to alternative medicine mainly in the form of health foods such as amino acids, lipids, carbohydrates, plants, seaweeds, insects, bacteria, yeasts and mushrooms. Such mushrooms as *Lentinula edodes*, *Ganoderma lucidum* and *Grifola frondosa* are commercially available. *Agaricus brasiliensis* (*A. blazei ss. Heinemann*) is a health food that has received recent attention. *A. brasiliensis* has been reported to improve symptoms of lifestyle-related diseases including obesity, hypertension and diabetes, and to have anti-inflammatory, antitumor, cancer inhibitory and immuno-enhancing effects (13–18). However, many reports were either animal studies or clinical studies with few cases.

Many mushrooms, also called as macrofungi, are classified as higher-order microorganisms, Basidiomycota. To discuss the functions of Basidiomycota, it is important to compare them under the same conditions, including not only the species but also the strain, as well as methods of cultivation and processing. Basidiomycota products involve mycelia, spores and fruit bodies in

each species. The fruit body and the mycelium are distributed widely in foods. To maintain the manufacturing process, the mycelium is superior to the fruit body; however, its components are known to be quite different. There are many ways to obtain the fruit body, e.g. collecting naturally grown mushrooms from hills and fields, and outdoor or indoor cultivation.

Agaricus brasiliensis KA21 used in this study is a fruit body cultivated outdoors in Brazil. Fruit bodies were air dried by a ventilator with a blowing temperature lower than 60°C to maintain their enzyme activities. We have recently examined the structure and antitumor activity of polysaccharide fractions of the fruit body and concluded significant contribution of the highly branched 1,3-β-glucan moiety on the activity. We also prepared the cold and the hot water extracts (AgCWE and AgHWE) and examined on a murine diabetic model C57Bl Ksj-db/db, and found that AgCWE showed much stronger pharmacological activity to this model. These facts strongly suggested that pharmacological action of cold water extract differ from that of hot water extract. We have also shown that the cold water extract contains enzymes such as polyphenol oxidase and peroxidase (19–25). Table 1 shows the general constituents of *A. brasiliensis* KA21. KA21 has high protein and fiber content. It also has high levels of vitamins B1, B2, B6, niacin, pantothenic acid, folic acid and biotin. It contains many minerals including large amounts of iron, potassium, phosphorus, magnesium, zinc and copper, and certain amounts of manganese and selenium. In addition, it contains detectable concentrations of vitamin D as it is cultivated under the sunlight.

To successfully achieve and maintain food safety for citizens, laws related to foods have become strictly controlled. Recently, medical doctors in National Cancer Center Hospital East in Japan reported three cases of severe hepatic damage, taking *A. blazei* extract (26). They mentioned it is necessary to evaluate many modes of complementary and alternative medicines, including the *A. blazei* extract, in rigorous, scientifically designed and peer-reviewed clinical trials. Very recently we have experienced evacuation of one health food originated from *A. brazei*, because of inducing genotoxicity in experimental animals. Ministry of Health, Labor and Welfare reported it is only the case of one product and the molecular mechanisms are under investigation. It is also simultaneously reported that other related products did not show such toxicity. Agaritine is a well known toxic metabolite of agaricaceae, such as *Agaricus bisporus*, and the relationship between agaritine content and the toxicity has attracted attention. In any case, function as well as safety of products originated from macrofungi, especially agaricaceae should be precisely examined as much as possible.

Thus, to safely and effectively use alternative medicine including *A. brasiliensis*, analysis at the molecular level by basic research and proving their effects by clinical research are important. In a human safety study, we found that long-term intake of the fruit bodies of *A. brasiliensis* KA21 cultivated outdoors had no adverse effects (22). In the present study, we demonstrated the immunomodulating effect of *A. brasiliensis* KA21 both by animal and human studies. As described earlier, the fruit body contained many enzymes even after the drying process, and cold and hot water extracts were prepared and administered orally to examine

Table 1. Composition of *A. brasiliensis* KA21

Energy	288.00 kcal
Protein	38.50 g
Fat	2.60 g
Carbohydrate	27.70 g
β-glucan	12.4 g
Fiber	20.60 g
Sodium	8.40 mg
Calcium	22.50 mg
Iron	10.10 mg
Potassium	2920.00 mg
Phosphorus	952.00 mg
Magnesium	96.50 mg
Zinc	7.87 mg
Copper	7.67 mg
Manganese	0.825 mg
Iodine	0
Selenium	88.00 μg
Arsenicum	0.48 ppm
Cadmium	2.01 ppm
Plumbum	0.13 ppm
Hydrargyrum	0.18 ppm
Total chromium	0 μg
Vitamin in A (total caronene)	0
Vitamin B (total caronene)	
Vitamin B1 (Thiamin)	0.63 mg
Vitamin B2 (Riboflavin)	3.04 mg
Vitamin B6	0.54 mg
Vitamin B12	0 μg
Niacin	33.50 mg
Pantothenic acid	22.90 mg
Folic acid	230.00 μg
Biotin	123.00 μg
Total vitamin C (Total c acid)	0 mg
Vitamin D	56.7 μg
Vitamin E (Total tocopherol)	0
Vitamin K1 loquinone)	0
Agaritine	15.3 ppm

Note: In 100 g dry weight, measured by Japan Food Research laboratories.
Agaritine was measured by MASIS laboratories by HPLC method.

immunomodulation in mouse models. Drinking such cold water extracts of *A. brasiliensis* is a traditional custom in Brazil. In the clinical study, we determined the weight, body mass index (BMI), percentage body fat, percentage visceral fat and blood biochemical levels [total protein, blood glucose, cholesterol, neutral fat, glutamate oxaloacetate transaminase (GOT), glutamate pyrvic transaminase (GPT) and glutamyl transferase (γ-GTP)], and natural killer (NK) cell activity before and after administration of *A. brasiliensis* KA21. Analysis of the data from the viewpoint of mibyou is also included.

Methods

Agaricus brasiliensis Fruit Bodies

Strain KA21 was cultivated outdoors in Brazil, and its fruit bodies were washed and dried using hot air at 60°C or lower.

Measurement of Ingredients

All ingredients except for agaritine were measured by Japan Food Research Laboratories, Shibuya, Tokyo using the standard protocols recommended by the Resources Council, the Science and Technology Agency of Japan. The concentration of agaritine was measured by HPLC/MS/MS by MASIS Inc, Minamitusgaru, Aomori.

Preparation of Hot Water Extract (AgHWE) and Cold Water Extract (AgCWE) of A. brasiliensis

The fruit bodies of KA21 (100 g each) were ground using a domestic coffee mill, suspended in 0.1 g/ml physiological saline (Otsuka Pharmaceutical Co., Ltd), and extracted in an autoclave (120°C, 20 min) or with cold water (4°C, 1 day). The supernatant after centrifugation was designated as AgHWE or AgCWE. The extracts were kept frozen at −20°C until use.

Oral Administration to Mice

AgHWE and AgCWE prepared by the earlier-described method were administered to mice orally for 2 weeks, and cell count and cell population were determined.

Murine Tumor Model

Solid form tumor: Sarcoma 180 cells (1×10^6/mouse) were subcutaneously administered to the groin of ICR mice on day 0. AgHWE or AgCWE was orally administered (p.o.) daily for 35 days. Standard β-glucan, sonifilan (SPG) was administered intraperitoneally on days 7, 9 and 11. After 35 days, the mice were sacrificed and the weight of the solid tumor was measured.

Inflammatory Cytokine Production in Primed Mice

Balb/c mice were primed with a standard β-glucan, SCG (200 μg/mouse) from *Sparassis crispa* on day 0, and AgHWE or AgCWE was orally administered daily for 1 week. One week later, bacterial lipopolysaccharide (LPS, 10 μg/mouse) was administered intravenously, serum was collected 90 min after the LPS administration, and serum TNF-α and IL-6 expression levels were measured with ELISA. Antibodies and standards were purchased from Pharmingen Ltd.

Concanavalin A-Induced Hepatic Injury in Mice

AgHWE or AgCWE were orally administered for several days in mice. One day after the final administration, Concanavalin A (Con A) was intravenously administered to induce liver injury. Interleukin 6 levels in sera were measured 3 h after Con A administration. GOT and GPT were measured 24 h after Con A administration.

Clinical Research in Humans

Research was performed on 31 healthy subjects who were not taking any medication prior to or at the time of the study. We explained the study to them in writing, and obtained informed consent to use the test results. The subjects were divided into three groups, group 2 and group 3 (total 20 subjects) were administered the normal dose, and group 1 (11 subjects) were administered a 3-fold higher dose (safety clinical study group) of *A. brasiliensis*.

Group 1. For 6 months from May 31 to November 26, 2004, the 11 subjects (mean age 43.6 ± 12.6 years, male 6, female 5) were asked to take 30 tablets/day (divided into three administrations; each tablet contained 300 mg of *A. brasiliensis*), which is three times the normal dose. Then, we measured and analyzed the subjective changes in their condition, liver function (GOT, GPT, γ-GTP), renal function [blood urea nitrogen (BUN), creatinine] and nutritional status (total protein).

Group 2. For 3 months from April 12 to July 8, 2005, 12 subjects (mean age 45.3 ± 8.1 years, male 9, female 3) were asked to take the normal dose of 10 tablets/day (divided into two administrations; each tablet contained 300 mg of *A. brasiliensis*). Then, we measured body weight, BMI, percentage body fat, percentage visceral fat and blood biochemical levels (total protein, blood glucose, cholesterol, neutral fat, GOT, GPT and γ-GTP).

Group 3. For 3 months from May to August, 2005, 8 subjects (mean age 22.3 ± 0.5 years, male 6, female 2) were asked to take the normal dose, and immune function (NK cell count, NK cell activity) was measured. In the measurement of immune function, we divided the eight subjects into two groups in a double-blind manner, *A. brasiliensis* group and placebo group, administered

10 tablets/day (divided into two administrations; each tablet contained 300 mg of *A. brasiliensis*) for 7 days, and determined NK cell count and NK cell activity in peripheral blood. After two-month drug withdrawal, the same study was conducted with the tablets exchanged (crossover). We analyzed the cell fraction in peripheral blood and regarded mononuclear cells with $CD3^-CD16^+CD56^+$ as NK cells. Following the usual method, we measured NK cell activity by 4 h ^{51}Cr-release assay using K562 tumor cells as targets, at an effector/target ratio (E/T) = 20 or 10 (the mixing ratio of mononuclear cells and K562 cells is 20 or 10).

Statistical Analysis

Paired *t*-test was used to evaluate statistical significance. $P<0.05$ was considered significant in all analyses.

Results

Chemical Analysis of *A. brasiliensis* KA21 for Safety Assessment

Before starting animal and human experiments, the chemical composition and additives were screened. The chemical composition and nutrients are shown in Table 1. Recently, a major toxic compound of agaricaceae 'agaritine' has attracted attention by showing tumor-promoting activity in rats. The agaritine content of *A. brasiliensis* KA21 was measured and it was as low as 15.3 ppm. Heavy metals, such as lead and mercury were lower than the detection limit. Three hundred types of pesticides were measured and none was detected (data not shown).

β-glucan content of *A. brasiliensis* KA21 was 12.4 g 100 g^{-1} measured by Japan food research laboratories. We have already precisely examined the structure of polysaccharide fractions of KA21, and the major structure of β-glucan showing immunomodulating activity was determined to be β-1,6-linked glucan with highly branched β-1,3-segment (20).

Vitamin D is a well known vitamin of macrofungi and KA21 contained 56.7 μg 100 g^{-1} (= ca. 2250 IU 100 g^{-1}). Same strain, cultured inside the house did not contain detectable concentration of vitamin D (data not shown). It is well known that concentration of vitamin D is strongly dependent on sunlight exposure. Vitamin D content of KA21 well reflected the culture condition of outdoor and under the sunlight.

From these data, *A. brasiliensis* KA21 was found to be chemically and analytically safe for animal and human studies.

Parameters and Effects on Experimental Animals

Effect on Normal Inbred Strains of Mice

For the animal experiments, AgCWE, AgHWE were prepared and examined. When AgCWE or AgHWE was administered orally at the dose of 20 mg/mouse to healthy mice (C3H/HeN) for 2 weeks, cell count in the thymus was not changed (data not shown), but that in the spleen was increased in the AgCWE group (Fig. 1).

Cells were doubly stained with CD4/CD8α, αβ/γδ, or CD3/B220, and the ratios of cell populations were calculated after measurement with a flow cytometer. No notable changes were seen in the thymus (data not shown), whereas the ratio of $CD4^+$ in the spleen was increased significantly in the AgHWE group (Fig. 1).

Antitumor Activity of Orally Administered AgCWE and AgHWE in Sarcoma 180 Transplanted Mice

We evaluated the antitumor effect of *A. brasiliensis* on Sarcoma 180 solid tumor, which is the standard system to measure antitumor effects in mice. Sonifilan (SPG) was used as standard material. Oral administration of

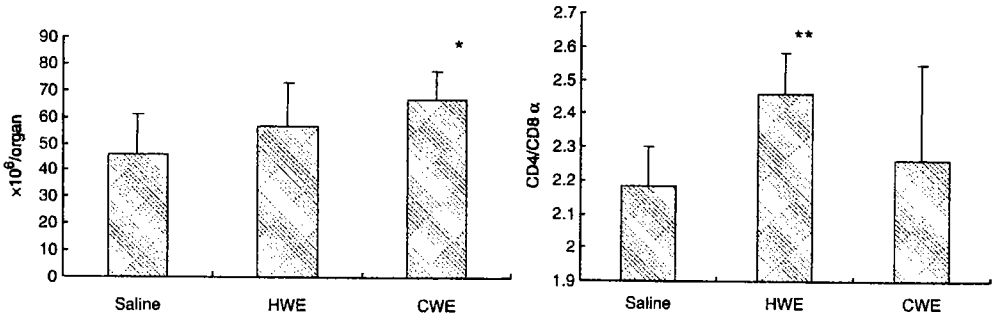

Figure 1. Cell number and population of splenocytes from AgHWE or CWE p.o. mice. AgHWE, CWE or saline (200 μl/mouse, 1 day, 1 shot), was p.o. administered to C3H/HeN mice for 14 days. The splenocytes were collected from each group of mice on day 14. Total cell number was counted with a hemocytometer (left). CD4/CD8α were measured by flow cytometory (right). The results represent the means ± S.D. $*P<0.05$, $**P<0.01$ compared with control by Student's *t*-test.

AgCWE or AgHWE for 35 days led to the suppression of tumor growth (Table 2).

Protection against Concanavalin A-Induced Liver Injury by Orally Administered AgCWE and AgHWE in Mice

The intravenous administration of Con A, a plant lectin, triggers acute hepatopathy in mice. We administered oral AgCWE or AgHWE as pretreatment, and then assessed the effects of Con A on hepatopathy. When 200 µl of AgCWE or AgHWE was administered for 7 days as pretreatment, GOT was found to decrease significantly in the AgCWE group. A similar trend was seen in the AgHWE group. When the dose was increased to 600 µl and administration was continued for 7 days, the effect became more notable (Fig. 2). GPT was decreased in a similar manner (data not shown). Similar studies were performed using different forms of administration and several mouse lines, and all cases showed a decreasing trend. Together, the results show that *A. brasiliensis* KA21 protects mice from hepatic injury.

Table 2. Antitumor effect of *A. brasiliensis* extracts on solid form of Sarcoma 180 in ICR mice

Name	Dose (mg)	Times	Route	CR/n	Tumor weight mean/SD (g)	% Inhibition	*t*-test
Control				0/12	8.6±4.3	0.0	
SPG	0.1	3	i.p.	7/11	0.4±1.1	95	<0.001
Control				0/10	15.0±6.5	0	
AgCWE	2	35	p.o.	0/10	9.6±6.5	36	<0.05
AgHWE	2	35	p.o.	0/10	7.9±2.5	47	<0.01

Note: Dose, per mouse; times, day 7, 9, 11; CR/n, Number of tumor free mice/total mouse. SPG, Standard β-glucan as positive control.

Protection of Multiple Organ Failure Induced by Lipopolysaccharide by Oral Administration of A. brasiliensis *KA21*

Next, we investigated cytokine production induced by the administration of bacterial endotoxin, LPS, an agent that induces multiple organ failure in severe infections, to determine the hepatocellular protective effect of AgCWE and AgHWE. The levels of TNF-α and IL-6 generated by LPS administration were decreased in both groups (Fig. 3), indicating that *A. brasiliensis* controls the level of cytokine production to protect organs.

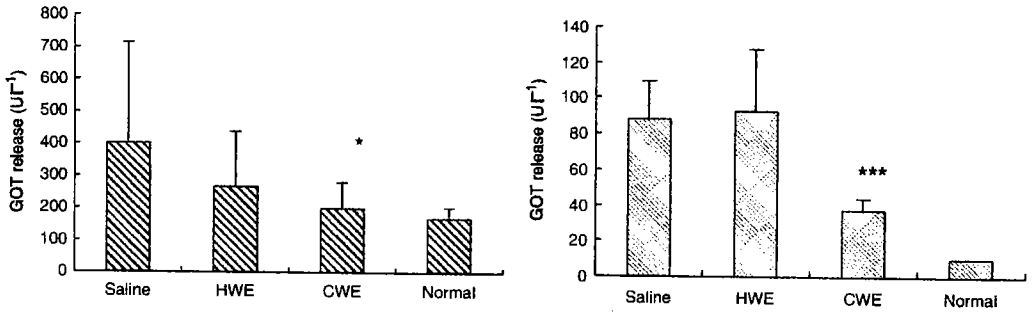

Figure 2. Effect of AgCWE or HWE p.o. on Con A-Induced liver injury. (Left) AgHWE or CWE (200 µl/mouse) was p.o. administered to Balb/c mice for 7 days. Con A (20 mg kg^{-1}) was iv administered on day 7 and the sera were prepared 24 h later from each group of mice. Results are expressed as the mean±SD $^{*}P<0.05$ compared with control by Student's *t*-test. ($N=7$). (right) AgHWE or CWE (600 µl/mouse) was p.o. administered to Balb/c mice for 7 days. Con A (20 mg kg^{-1}) was iv administered on day 7 and the sera were prepared 24 h later from each group of mice. Results are expressed as the mean±SD $^{***}P<0.001$ compared with control by Student's *t*-test. ($N=3$).

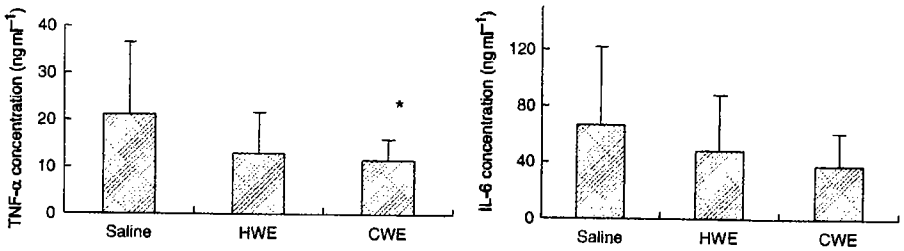

Figure 3. Effect of oral *A. brasiliensis* on LPS-induced cytokine production. β-Glucan (SCG, 200 µg/mouse) was i.p. administered to Balb/c mice on day 0. AgHWE or CWE was p.o. administered to these mice for 7 days. LPS (10 µg/mouse) was iv administered as a triggering reagent on day 7 and the sera were prepared 1.5 h later from each group of mice. IL-6 and TNF-α was measured by ELISA. Results are expressed as the mean±SD $^{*}P<0.05$ compared with control by Student's *t*-test. (left) TNF-α, (right) IL-6.

Clinical Research

Safety of A. brasiliensis

Before determining the safety of *A. brasiliensis* KA21, a normal dose was administered for 3 months to 13 subjects as a preliminary experiment and measured changes of general clinical parameters. Mean body weight (71.2 → 70.9 kg), size of waist (85.4 → 83.5 cm), percentage body fat (34.4–33.0%) and BMI (27.8–27.6) did not show any clinical sign of illness by taking it. Thus to precisely determine the safety of *A. brasiliensis* KA21, a dose of three times higher than the normal dose was administered for 6 months to 11 subjects (group 1, see 'Methods'), and subjective changes in conditions, liver function, renal function and nutritional conditions were measured and analyzed. After measuring the biochemical parameters, we confirmed no statistically significant difference before and after administration, and no side effects caused by long-term administration (Table 3).

Effect of A. brasiliensis *on Biochemical Parameters related to Adiposis and Diabetes*

In order to evaluate the effect of *A. brasiliensis* KA21 on lifestyle-related diseases, the normal dose was administered to 12 subjects (group 2, see 'Methods') for 3 months and comparison of clinical biochemical data was made. The results are as follows: (i) Significant decreases were seen in body weight and BMI ($P<0.01$ each) after administration (Figs 4 and 5). (ii) Significant decreases were observed in percentage body fat ($P<0.01$) and percentage visceral fat ($P<0.01$) after administration (Figs 6 and 7). (iii) Significant increase was found in total protein level ($P<0.03$) after administration (Fig. 8). (iv) Significant reduction was seen in blood glucose level ($P<0.02$) after administration (Fig. 9).

Table 3. Safety of *A. brasiliensis* KA21 in human volunteers

Biochemical parameters	Before (mean ± SD)	After (mean ± SD)	Statistics (*P*-value)
Total protein ($g dl^{-1}$)	7.50 ± 0.16	7.41 ± 0.25	0.31
BUN ($mg dl^{-1}$)	15.81 ± 5.93	13.45 ± 2.25	0.12
Creatinine ($mg dl^{-1}$)	0.92 ± 0.21	0.90 ± 0.20	0.19
GOT (μl^{-1})	18.8 ± 4.75	19.8 ± 4.40	0.10
GPT (μl^{-1})	15.7 ± 6.90	16.3 ± 4.90	0.52
γ-GTP (μl^{-1})	35.4 ± 29.6GTP	35.9 ± 30.1	0.89

($N=11$).

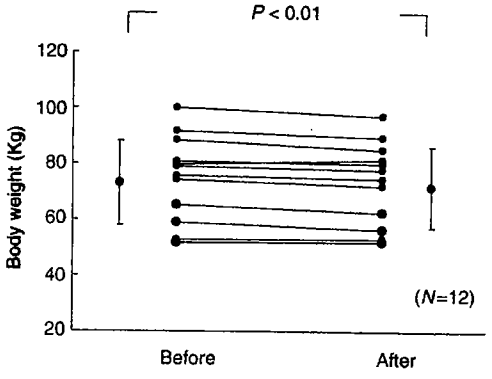

Figure 4. Effect of *A. brasiliensis* on body weight. Experimental protocol was shown in 'Methods'.

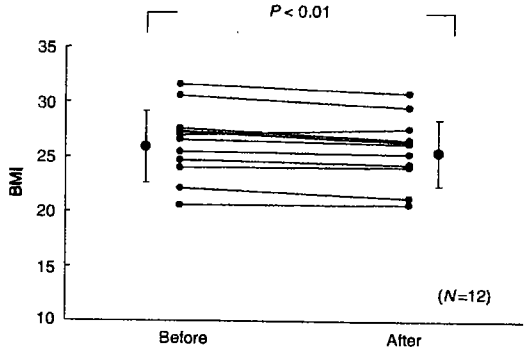

Figure 5. Effect of *A. brasiliensis* on BMI. Experimental protocol was shown in 'Methods'.

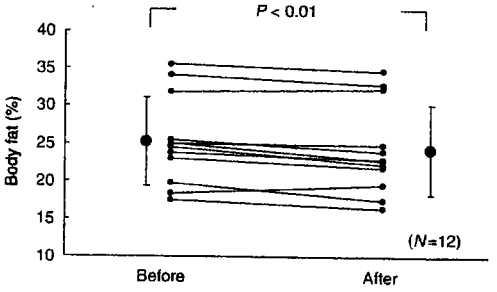

Figure 6. Effect of *A. brasiliensis* on percentage body fat. Experimental protocol was shown in 'Methods'.

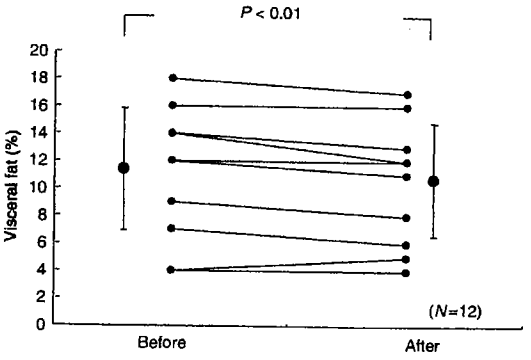

Figure 7. Effect of *A. brasiliensis* on percentage visceral fat. Experimental protocol was shown in 'Methods'.

In order to analyze the data more precisely, the subjects were divided according to total cholesterol level into a normal value group (T-CHO < 200 mg/dl) and a mibyou (slightly sick) value group (T-CHO ≥ 200 mg/dl) for comparison. No change was observed in the T-CHO < 200 mg/dl group before and after administration, whereas a decrease was seen in the T-CHO ≥ 200 mg/dl group after administration (Fig. 10).

The subjects were divided according to blood neutral fat level into a normal value group (TG < 120 mg/dl) and a mibyou value group (TG ≥ 120 mg/dl) for comparison. No change was observed in the former, whereas a decrease was observed in the latter after administration (Fig. 11).

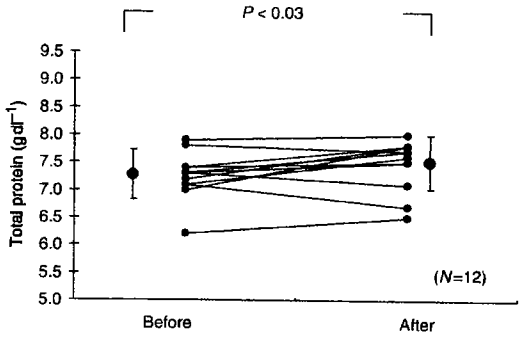

Figure 8. Effect of *A. brasiliensis* on total protein level. Experimental protocol was shown in 'Methods'.

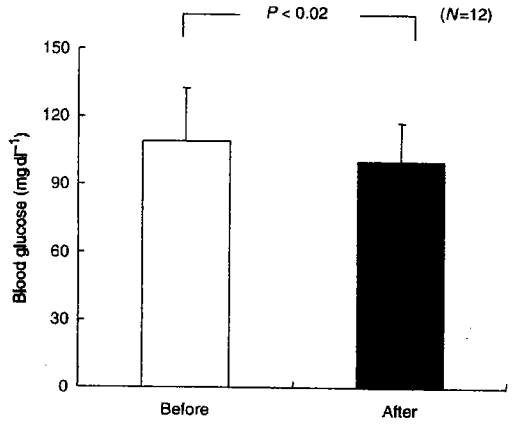

Figure 9. Effect of *A. brasiliensis* on blood glucose level. Experimental protocol was shown in 'Methods'.

Improvement of Liver Function by A. brasiliensis

To determine liver function, we compared GOT, GPT and γ-GTP values of the earlier mentioned subjects shown in the previous section. When comparison was made among all 12 subjects, no differences were seen before and after administration (Fig. 12). By contrast, after the subjects were divided into normal and mibyou according to GOT level, the average value of GOT in the normal value group (GOT < 25 IU l^{-1}) was found to increase slightly after administration, whereas that in the mibyou value group (GOT ≥ 25 IU l^{-1}) was found to decrease after administration, although the difference was not statistically significant (Fig. 13). The average value of GPT was increased in the normal value group (GPT < 25 IUl^{-1}) after administration, whereas that in the mibyou value group (GPT ≥ 25 IUl^{-1}) was decreased slightly after administration, the difference being not statistically significant (Fig. 14). The average value of γ-GTP was decreased slightly in the normal value group (γ-GTP < 30 IU l^{-1}) after administration, whereas that in the mibyou value group (γ-GTP ≥ 30 IU l^{-1}) was almost unchanged (Fig. 15).

Taken together, we determined that both lipid and blood glucose levels showed a decreasing trend for

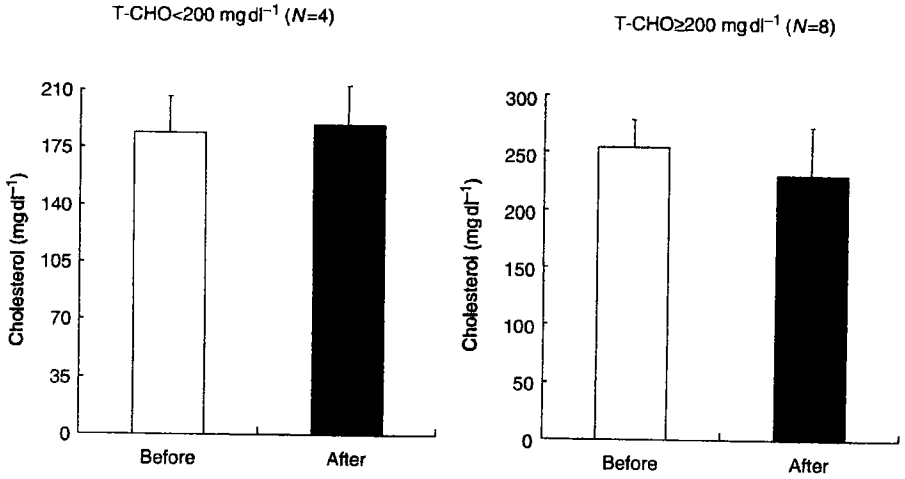

Figure 10. Effect of *A. brasiliensis* on blood cholesterol level from the viewpoint of Mibyou. Experimental protocol was shown in 'Methods'.

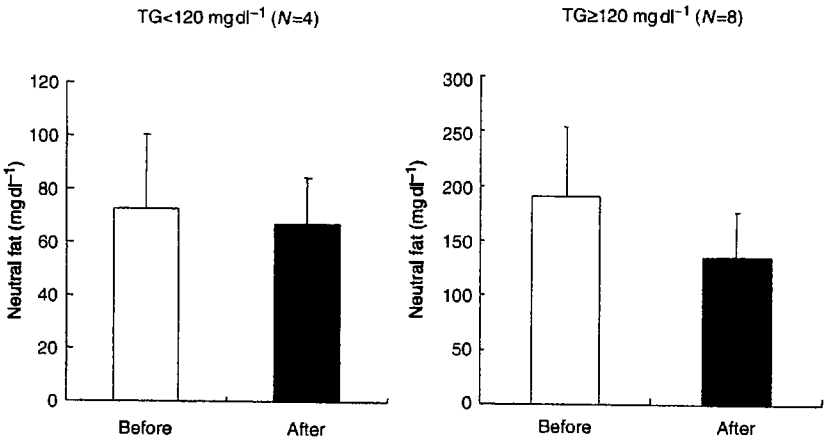

Figure 11. Effect of *A. brasiliensis* on neutral fat level from the viewpoint of Mibyou. Experimental protocol was shown in 'Methods'.

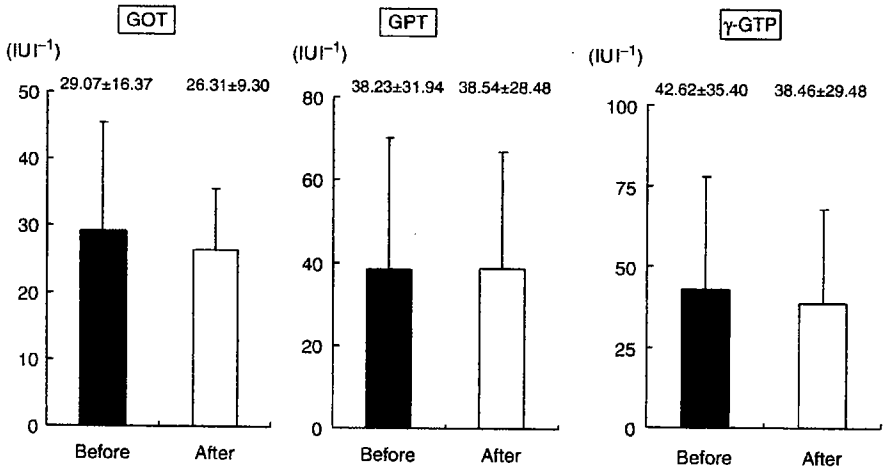

Figure 12. Effect of *A. brasiliensis* on liver function. Experimental protocol was shown in 'Methods'.

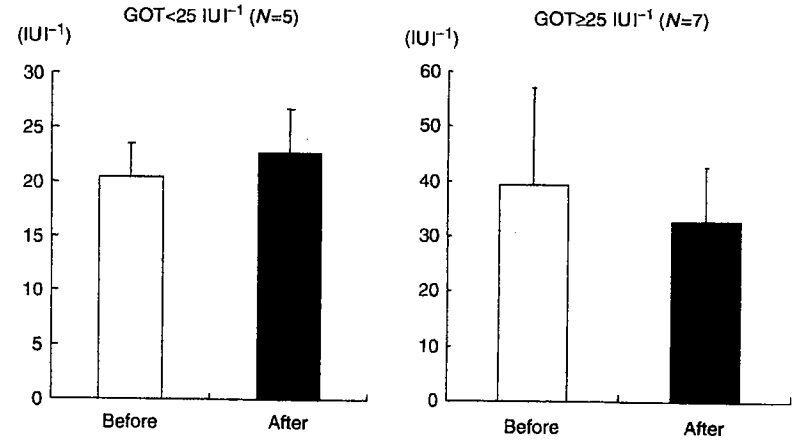

Figure 13. Effect of *A. brasiliensis* on liver function (GOT Value) from the viewpoint of mibyou. Experimental protocol was shown in 'Methods'.

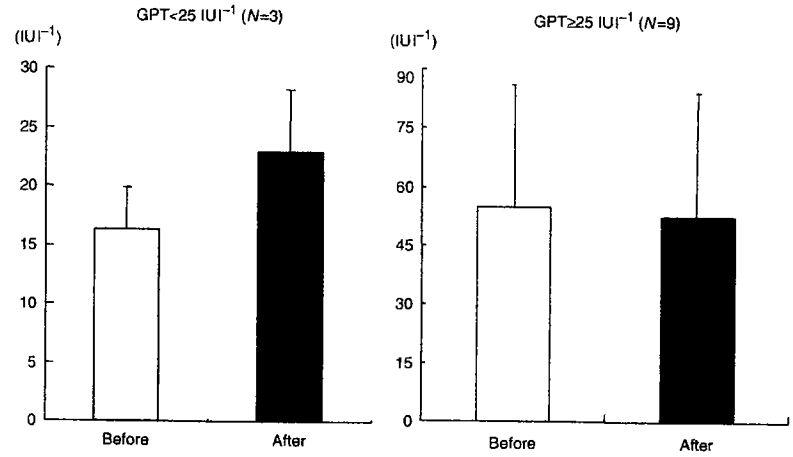

Figure 14. Effect of *A. brasiliensis* on liver function (GPT Value) from the viewpoint of mibyou. Experimental protocol was shown in 'Methods'.

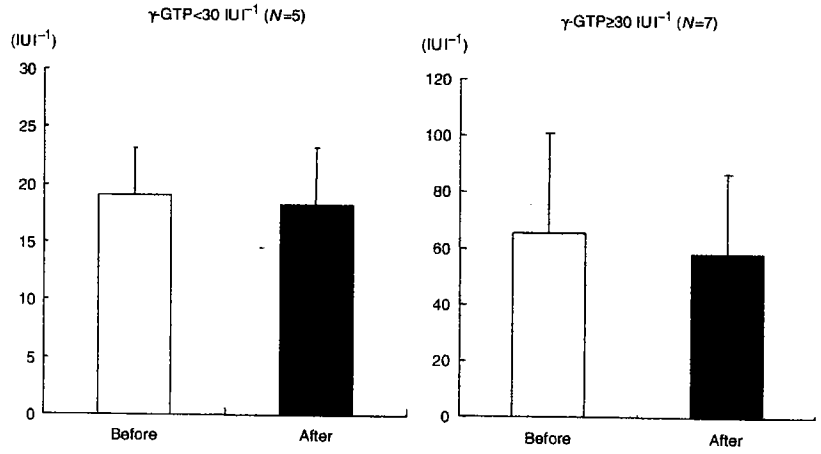

Figure 15. Effect of *A. brasiliensis* on liver function (γ-GTP Value) from the viewpoint of mibyou. Experimental protocol was shown in 'Methods'.

lifestyle-related diseases. In addition, an improvement in liver function was noted.

Modulation of Natural Killer Cell by A. brasiliensis

In order to evaluate the effect of *A. brasiliensis* KA21 on immune function, NK cell number and function were examined by eight subjects in a double-blinded experimental protocol shown in 'Methods' (group 3, see 'Methods'). The normal dose or placebo was administered to eight subjects for 7 days and NK cell number and activity in peripheral blood was compared as follows.

Effect of A. brasiliensis *on NK Cell Count*

Comparison of NK cell count before and after administration, and comparison between the *A. brasiliensis* group and placebo group were made, and no statistically significant differences were observed (Fig. 16).

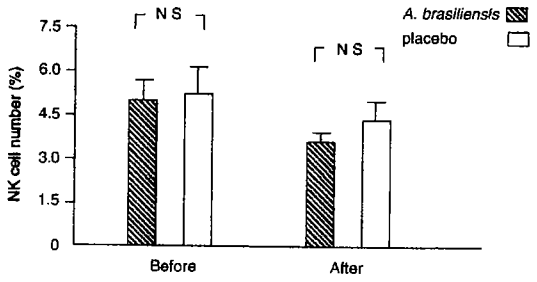

Figure 16. Comparison of NK cell count between groups before and after administration of *A. brasiliensis*. Experimental protocol was shown in 'Methods'.

Augmentation of NK Cell Activity by A. brasiliensis *KA21*

Before administration, no significant differences were observed between *A. brasiliensis* group and placebo group

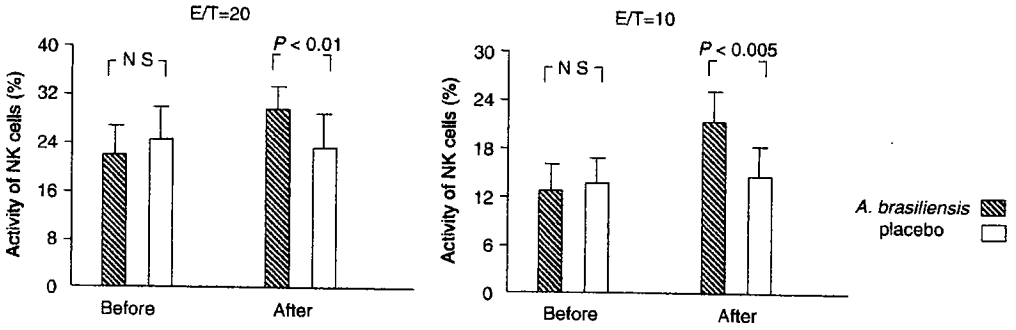

Figure 17. Effect of *A. brasiliensis* on NK cell activity. (Comparison between *A. blazei* group and placebo group). Experimental protocol was shown in 'Methods'.

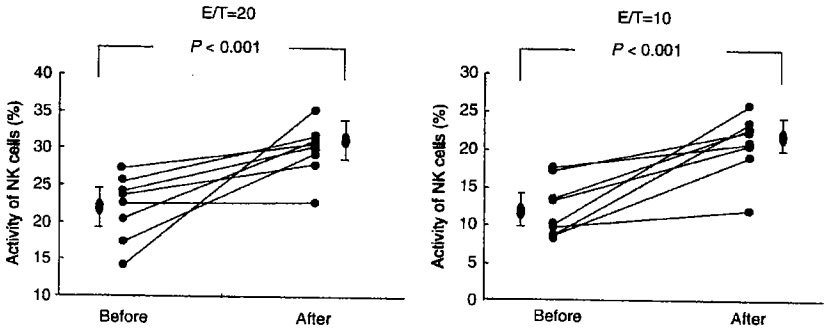

Figure 18. Comparison of NK cell activity before and after administration of *A. brasiliensis*. Experimental protocol was shown in 'Methods'.

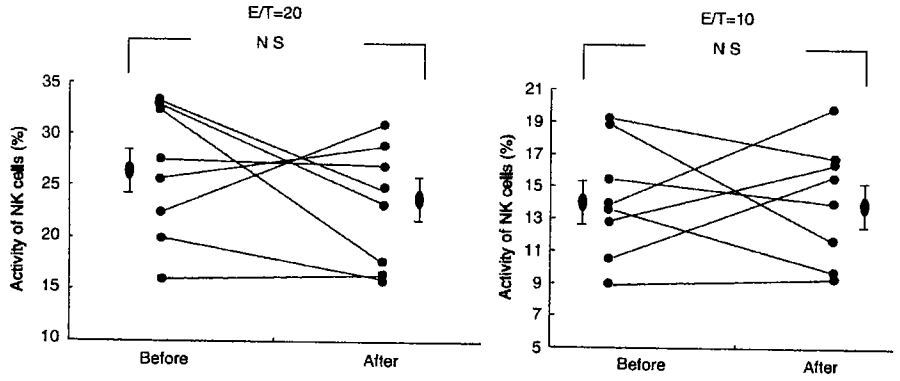

Figure 19. Comparison of NK cell activity before and after administration of placebo. Experimental protocol was shown in 'Methods'.

(Fig. 17 left). After administration, there were significant differences between the two groups, with $P<0.01$ for the E/T = 20% group and $P<0.001$ for the E/T = 10% group (Fig. 17 right). Figs 18 and 19 show individual changes in NK cell activity after administration of *A. brasiliensis* (Fig. 18) and placebo (Fig. 19) groups. NK cell activity was increased significantly in *A. brasiliensis* groups, with $P<0.001$ for the E/T = 20% group and $P<0.001$ for the E/T = 10% group. Meanwhile, NK cell activity was not increased significantly in the placebo group after administration.

Discussion

Japan is rapidly becoming a super-aging society, and such issues as decreased workforce, consumption and tax revenues, and increased international competition

among neighboring Asian nations are emerging. As a dramatic increase in the number of elderly patients is inevitable, the social security system is expected to become financially strained, and patient and consumer awareness of their rights will be enhanced because of the increased financial burden levied on them. Whereas genetic disposition is said to be involved in the development of lifestyle-related conditions and diseases, such as diabetes, hyperlipidemia and cancer, several other factors also determine their development; therefore, lifestyle is closely related to the development of such conditions and diseases. On the other hand, there is a need to reduce the significantly elevated medical expenses in the future. There are discussions as to whether we should pay medical expenses to aid people who do not practice a healthy lifestyle. The number of people who are not sick yet not healthy, that is, 'in poor health' or 'mibyou', is increasing at an accelerated pace (27,28). It is difficult to maintain regular eating habits in stress-laden daily life. Improvement of diet by consuming functional foods seems to contribute to the health improvement of people with poor health, as well as to the prevention of the development of lifestyle-related diseases.

There are many functional foods in Japan and they are expensive for customers, thus accurate information is needed to select the best food for each customer. All the parameters of safety, cost performance, evidence of function, as well as taste are important to disclose.

Mushrooms have been a part of oriental medicine for hundreds of years as being beneficial for health. Most traditional knowledge about the medicinal properties of mushrooms comes from the Far East, Japan, China, Korea and Russia. The most striking evidence is that lentinan from *L. edodes*, sonifilan from *Schizophyllum commune* and krestin from *Coriorus versicolor* have been approved for anticancer drugs mediated by immune stimulation. A great many mushroom products are on the market as health promoting foods, and basic and clinical researches of these products have been performed continuously (29–41).

Currently, there are 80 000 known fungal species in the world. It is surmised that 1 500 000 species exist, including undiscovered species. These fungi are classified by kingdom, phylum/division, class, genus and species. Many fungi are classified into Basidiomycota or Ascomycota, whereas others are also classified into the kingdom Protozoa or kingdom Chromista. Fungi include mushrooms, molds and yeasts, which have significantly different appearance and sizes. As mushrooms are too large to be considered microorganisms, they are referred to as macrofungi. Lichens of which two or more microorganisms live in a symbiotic relationship are also included. Fungi exhibit both the sexual form (for example, morphology of mushroom) and the asexual form for regeneration (for example, morphology of mycelium) and either form is used depending on surrounding environmental changes; however, the existence of both forms (holomorph) is not known for all fungi. Their nomenclature is also characteristic. The background of the discovery of a fungus is reflected in its name and different names may be given depending on whether the fungus exhibits the sexual form (teleomorph) or the asexual form (anamorph) of regeneration. Fungi, particularly mushrooms, are 'cultivated' and distributed products, and detailed analysis of their components has been performed. In the Standard Tables of Food Composition in Japan (Fifth Edition), 36 foods are classified as 'mushrooms'. The representative nutritional composition of mushrooms includes fiber, glucose and sugar alcohols, organic acids, fatty acids, inorganic substances, vitamins, free amino acids, bitter and pungent components, flavor components, enzymes, biophylactic substances, pharmacologically active substances and toxic components. Moreover, molds and yeasts are related to some fermented foods. A variety of foods including sake (rice wine), miso (bean paste), soy sauce, cheese and katsuobushi (dried bonito) are manufactured with the help of eukaryotic microorganisms. Fungus produces many secondary metabolites that are used as drugs or raw material for drugs, an example of which is penicillin.

As regards edible mushrooms, some are consumed raw, and cultivated hypha and culture broth are distributed as supplements after processing. Although they are from the same fungus, there is no proof that they contain the same components as the cultivated fruit bodies. In the early 1980s, we performed animal studies to compare the macromolecular components of *G. frondosa* fruit bodies, mycelia and fermented products. That the quantities and quality of components contained in each extract differed considerably was also reflected in the activity (29–32). *Grifola frondosa* has been well studied in Japan and in other countries. Interestingly, the major active component differs depending on the study group (33–37). Comparing mushrooms and mycelia at the product level, it was found that live fungus differs from dried products. From the viewpoint of stable supply, the dried product is desirable, but its components change according to the drying method. It is likely that the components differ if the 'fungal strain' differs. Thus, one type of mushroom may vary greatly when processed as food or other products. When we want to discuss or evaluate components and pharmacologic action, we need to conduct comparisons under detailed conditions, especially if we perform animal experiments.

Agaritine (N-[γ-L-(+)-glutamyl]-4-hydroxymethylphenylhydrazine) was identified in fruit bodies of cultivated mushrooms belonging to the genus *Agaricus*, including commerce *A. bisporus* and closely related species (42–46). 4-(hydroxymethyl) benzenediazonium ion that had mutagenicity is believed to be formed when agaritine is metabolized. Agaritine is most prevalent, usually occurring in quantities between 200 and 400 $\mu g\,g^{-1}$ as

fresh weight, 1000–2500 $\mu g\,g^{-1}$ as dry weight in cultivated mushroom. Recently, agaritine in *A. brasiliensis* (*A. blazei*) sample and products was measured. These samples contained 112–1791 $\mu g\,g^{-1}$ of agaritine as dry weight (47). In the present study, we have detected only low concentrations of agaritine (15.3 ppm; 15.3 $\mu g\,g^{-1}$) in the preparation made of *A. brasiliensis* KA21. This value was <1/100 of the quantity of average values of *A. bisporus*. Agaritine content is known to be significantly varied depending on processing. Household processing (e.g. boiling, frying, microwave heating or drying) will reduce the agaritine content in *A. bisporus* by up to 50% or even more (48). Also, agaritine has recently been shown to be degraded oxygen dependent in water (42,43). There have been long discussing the toxicity and carcinogenicity of agaritine (44,45). However, the conclusion is still controversial. Toth and co-workers (46,49–51) undertook the work to assess the possible carcinogenic activity of the phenylhydrazines and related compounds in *A. bisporus*. Their studies indicated that most of phenylhydrazine and related compounds in the mushroom are carcinogenic in Swiss albino mice. The only compound that was tested negative was agaritine, a finding that significantly muddled the interpretation of the carcinogenicity data. Also, these studies were the conservative risk model. In the absence of epidemiological data, no evaluation of carcinogenicity of agaritine to humans could be made.

We have analyzed *A. brasiliensis* KA21 from various aspects and reported the β-glucan, the enzymes of polyphenol oxidase, peroxidase and β-1,3-Glucanase. β-glucan content of *A. brasiliensis* KA21 was 12.4 g $100\,g^{-1}$ measured by Japan food research laboratories. We have already precisely examined the structure of polysaccharide fractions of KA21, and the major structure of β-glucan showing immunomodulating activity was determined to be β-1,6-linked glucan with highly branched β-1,3-segment (20). During that study we have prepared hot water extract, cold alkaline extract, and hot alkaline extracts and analyzed polysaccharide structure of all these fractions. Of much interest, all the fraction showed quite similar structural features that major linkage is β-1,6-linked glucan. From these data, major polysaccharide component in *A. brasiliensis* is β-1, 6-linked glucan, and it is consistent with the previous study. However, we have mentioned that antitumor activity needs β-1,3-linkages in addition to β-1,6-linkage based on the results of the limited chemical degradation study. However, this conclusion is still temporal and structural activity relations needed human studies.

This study showed that the fungus is rich in vitamins; as it is cultured outdoors, it contains detectable concentrations of vitamin D. Vitamin D is a well-known vitamin of macrofungi and KA21 contained 56.7 $\mu g\,100\,g^{-1}$ dry weight. In the parallel experiments, vitamin D was contained lower than the detection limit (0.7 $\mu g\,100\,g^{-1}$) in the mycelium of this fungi cultured in the liquid medium and the fruit body of *A. blazei* imported from China. Much differences of vitamin D in these products well reflected the culture condition of outdoors and under the sunlight. Relationship between vitamin D content and sunlight exposure has been demonstrated in various macrofungi (52). Based on the definition in the manual of Health Food Regulation in Japan, the food containing more than 1.5 $\mu g\,100\,g^{-1}$ (= 60 IU $100\,g^{-1}$) of vitamin D is defined as the food containing high vitamin D content. Considering the rule, KA21 is the food containing high concentration of vitamin D. Micronutrients such as vitamins and minerals promote the metabolism of waste products, carbohydrates and lipids via cellular activation, and improved insulin resistance by decreasing blood glucose. Fiber and unsaturated fatty acids decrease blood pressure and promote decholesterolization. KA21 also contained other micronutrients, thus it is good for health for variety of reasons.

Meanwhile, in an analysis of the active components in bupleurum root, a crude drug, we found that polyphenols polymerized by enzymes have a strong immunoenhancing effect (53–55). *A. brasiliensis* also has a number of enzymes related to the polymerization of polyphenols (23,24). Polyphenols polymerized by these enzymes may be active components in this fungus. In our clinical research, decreases in body weight, BMI, percentage body fat, percentage visceral fat and blood glucose level were noted and a tendency to decrease blood cholesterol level, blood neutral fat level, GOT, GPT and γ-GTP was observed in the mibyou value group. On the basis of the earlier results, among the components of this fungus, all the polysaccharides, enzymes, vitamins and minerals may be involved in the normalization of biochemical test results.

This study measured immune function in mice. When we compared the number and population of immunocompetent cells after administration of AgCWE or AgHWE to healthy mice orally for 2 weeks, it was found that the percentage of spleen $CD4^+T$ cells was increased in the AgHWE group and the number of spleen cells was increased in the AgCWE group. Furthermore, both AgCWE and AgHWE showed antitumor effects and AgCWE prevented Con A-induced hepatopathy and suppressed cytokine production induced by LPS. $CD4^+T$ cells are divided into type 1 helper T cells (Th1) and type 2 helper T cells (Th2) based on T-cell antigen stimulation, and Th1 is considered to be a more important contributor to the antitumor effect. Th1 is thought to infiltrate local sites well, demonstrate strong cytotoxicity and cytokine production ability, and induce complete tumor regression by locally inducing CTL, which has the ability to produce IFN-γ (56–58). It is likely that the antitumor effect of *A. brasiliensis* is closely related to the increase in $CD4^+T$ cell count.

As changes in immunocytes were demonstrated by the oral administration of *A. brasiliensis* in healthy mice, it is expected that the daily intake of *A. brasiliensis* may have preventive effects on immunoregulation failure.

Agaricus brasiliensis suppressed organ dysfunction accompanied by blood with excessively high cytokine levels, which is related to multiple organ failure. It is desirable that cytokines be produced at certain levels as needed. In these models, such as LPS-elicited cytokine production, *A. brasiliensis* controlled excessive cytokine production (Fig. 3). *A. brasiliensis* can not only promote but also control immunity, which is considered a desirable effect.

Among the effects of *A. brasiliensis* on immune function, we examined changes in the ratio of NK cells to peripheral mononuclear cells and NK cell activity in humans. Both the *A. brasiliensis* group and the placebo group showed no significant changes in the ratio and number of NK cells to peripheral mononuclear cells after 1-week administration. On the other hand, comparing the *A. brasiliensis* and placebo groups, NK cell activity was significantly enhanced by the administration of *A. brasiliensis*. When individual cases were examined, almost all cases showed increasing NK cell activity with the administration of *A. brasiliensis*, although there were differences in the degree of increase (Fig. 18).

The measurement of NK cell activity has been most widely used in both animal and human experiments, because NK cells play a critical role in natural immunology, and measurement of cytotoxicity is reliable for evaluation with good reproducibility (5). The immune function is affected by NK cells as well as various lymphocyte and humoral factors including antibodies, complement and cytokines. There have been several publications demonstrating products of macrofungi enhanced NK activity (59–63).

The effect of *A. brasiliensis* on the degree of NK cell activity enhancement varied significantly among individuals. It was recently clarified that effectiveness as well as the appearance of side effects with each medication were significantly different in each individual. This is explained partly by polymorphism and the linkage of CYP-related genes, a drug-metabolizing enzyme group (64,65). On the other hand, many causative genes have been discovered in immunity-related diseases, some of which are polymorphic. It is possible that polymorphism may be related to individual differences observed in the effects of *A. brasiliensis*. Research into receptors for mushroom components is not extensive. Dectin-1 was recently determined to be the receptor for cell wall β-glucan, a major component of mushrooms (66–68). The relationship between polymorphism of the receptor for pathogens and disease has been elucidated (69,70). The effects of *A. brasiliensis* and receptor gene polymorphism may be related. Further analysis is necessary in the future.

Through basic and clinical research, we confirmed that *A. brasiliensis* can help to improve symptoms of lifestyle-related diseases because of its anti-inflammatory, antitumor and immunoenhancing effects, and that *A. brasiliensis* is a useful health food to treat mibyou (primary prevention).

Very recently we have experienced recall of one health food originated from *A. brazei*, because of inducing genotoxicity in experimental animals. Ministry of Health, Labor and Welfare reported it is only the case of one product and the molecular mechanisms are under investigation. Based on the clinical examination shown in this study, KA21 is very safe for human health. Any adverse effect could not be detected in our study. We have also stated that content as well as pharmacological action is significantly influenced by culture conditions even in the same fungi, such as vitamin D content. In addition, proteins may be decomposed during processing. Much restricted regulation for each of the health foods might be needed for increasing human health. In any case, agaricaceae contained many species for functional foods, thus, much study should be needed continuously. This study helped to understand the mushrooms of agaricaceae are very safe and useful for human health.

Conclusion

(i) In basic research using a mouse model, we determined that *A. brasiliensis* has antitumor, anti-inflammatory and hepatocellular protective effects. It was suggested that the increase in the number of helper T cells and the enhancement of NK cell activity are related to these effects.

(ii) In clinical research on human volunteers, we found that *A. brasiliensis* decreased body weight, BMI, percentage body fat, percentage visceral fat and blood glucose level significantly, and reduced obesity. It also decreased blood cholesterol level and neutral fat level, normalized liver function and activated the immune function in mibyou patients (people with poor health).

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The Mushroom *Agaricus blazei* Murill Extract Normalizes Liver Function in Patients with Chronic Hepatitis B

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ABSTRACT

Background: Hepatitis B is a global health problem. Use of complementary and alternative medicine has been popular among patients with hepatitis B. This 1-year open-label pilot study aims to observe whether *Agaricus blazei* Murill extract improves liver function in patients with hepatitis B.

Methods: This study involved 12 months of clinical observation. Four (4) patients with hepatitis B who met the criteria (1) aged between 20 and 65 years; (2) being Chinese; (3) having been a hepatic B carrier (HBAg(+)) for more than 3 years; (4) alanine aminotransferase >100 IU/L; and (5) not taking lamivudine, α-interferon, or other drugs for hepatitis participated in the study with informed consent. The enrolled patients were given *Agaricus blazei* Murill (ABM) extract of 1500 mg daily for 12 months. The level of alanine aminotransferase was taken as the major outcome measurement.

Results: At the end of the study, the mean level of aspartate aminotransferase and alanine aminotransferase decreased from 246.0 (± standard deviation [SD] 138.9) to 61.3 (± SD 32.6) IU/L and 151.0 (± SD 86.9) to 46.1 (± SD 22.5) IU/L, respectively.

Conclusions: Our initial observation seems to indicate the potential benefit of ABM extract in normalizing liver function of patients with hepatitis B. Controlled studies with larger samples should be conducted in the future.

INTRODUCTION

Hepatitis B is a global health problem. Use of complementary and alternative medicine has been popular among patients with viral hepatitis. It is desirable to find a natural product that can help patients with hepatitis B with abnormal liver function.

Agaricus blazei Murill (ABM) is a mushroom and natural food, which has been used as a health care product for the prevention of a wide range of illnesses including cancer, diabetes, arteriosclerosis, and chronic hepatitis. It has been reported that ABM has beneficial effects in fighting cancer[1–3] and viruses,[4] improving insulin resistance in type 2 diabetes,[5] as well as enhancing production of antibodies by vaccines.[6,7] Chen et al.[6] have demonstrated that ABM extract might serve as an adjuvant in improving the efficacy of hepatitis B vaccines *in vivo*. Rich polysaccharides such as β-glucans are found to be the main constituents of ABM.[8,9] In view of the beneficial effects of ABM on patients with hepatitis B observed in our short pilot study, we conducted this 1-year follow-up clinical trial to examine whether ABM extract can improve liver function in patients with chronic hepatitis B.

METHODS

Study design and population

This was an open-label pilot study with no placebo given to match. The trial was conducted from August 1, 2004 through July 31, 2006 in Taipei Hospital, Taiwan. Four (4)

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patients with hepatitis B who met the criteria (1) aged between 20 and 65 years, (2) being Chinese; (3) having been a hepatitis B carrier (HBAg(+)) for more than 3 years, (4) alanine aminotransferase >100 IU/L; and (5) not taking lamivudine, αinterferon, or other drugs for hepatitis participated in the study. The protocol was approved by the Human Ethics Committee of our hospital. Informed consent was obtained from all 4 enrolled patients. All subjects were free to withdraw at any time during the course of the study.

Preparation of sample and treatment

ABM is a health care product popularly used in Taiwan. Our ABM extract, obtained from Eng Chiao Bio-Technology Co. Ltd., Taiwan, were extracted from dried fungal bodies of ABM according to the preset standard procedures with certificate of analysis given.[5] The subjects were given one capsule containing 500 mg of ABM extract three times each day for 12 months. This capsule was taken 30 minutes after eating.

Assessment

The level of alanine aminotransferases was used as the major outcome measurement. Blood samples were taken from the subjects once every 4 months during the study period. The side-effects and complications were also evaluated.

RESULTS

Figure 1 shows the changes in level of aspartate aminotransferases and alanine aminotransferases during the 12-month follow-up. All of these 4 cases received treatment that involved taking ABM extract.

Case 1, a 38-year-old male patient, had hepatitis B for 22 years. His initial levels of aspartate aminotransferases and alanine aminotransferases were 72 and 127 IU/L, respectively, which dropped to 43 and 63 IU/L, respectively, after 12 months. Case 2, a 22-year-old male patient, had hepatitis B for 4 years. His initial levels of aspartate aminotransferase and alanine aminotransferase were 125 and 227 IU/L, respectively, and decreased to 17 and 18 IU/L, respectively, at the end of the study period.

Case 3, a 65-year-old male patient, had been suffering from hepatitis B for 30 years with abnormal liver function. Both his aspartate aminotransferases and alanine aminotransferase levels exceeded 100 IU/L throughout these 30 years. Before the ABM treatment, his initial levels were 132 and 156 IU/L, respectively. No improvement was observed during the first 9 months of treatment, but aspartate aminotransferases and alanine aminotransferase levels eventually decreased to 69 and 97 IU/L, respectively, 1 year later.

Case 4 was a 54-year-old woman who had been a hepatitis B carrier for 25 years. General malaise, poor appetite, and abdominal fullness had been noted for 1 month. Her serum levels of aspartate aminotransferases and alanine aminotransferase were high at 275 and 414 IU/L, respectively, before taking the ABM extract. Soon after the treatment, she began to feel better with symptoms relieved, and the levels of aspartate aminotransferases and alanine aminotransferase became 58 and 67 IU/L, respectively, at the end of the study.

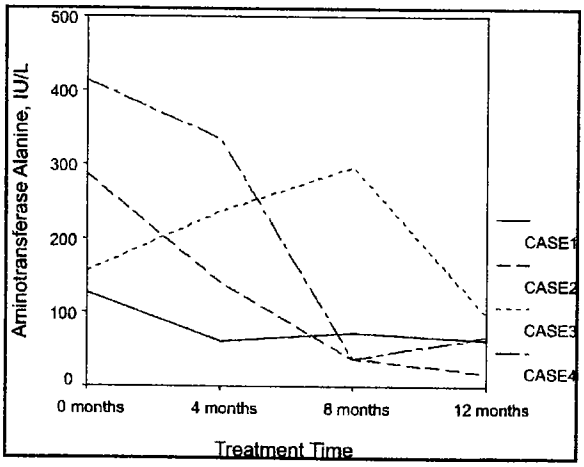

FIG. 1. Changes in levels of aspartate aminotransferase and alanine aminotransferases among four cases during 12-month follow-up.

Adverse effects

No major or minor adverse effects were noted during the 12 months of ABM treatment. The renal function was also evaluated and was within normal limits.

DISCUSSION

This 1-year clinical observation shows the potential benefits of ABM extract as a supplement for normalizing liver function in subjects with chronic hepatitis B.

Chronic hepatitis B is an escalating health problem. The recommended treatment regimen incurs considerable expenses, not to mention the side-effects and reduced efficacy in some patients. The serum level of liver enzymes is an important marker for evaluating the severity of the disease. Normalization of liver enzymes in patients with hepatitis B would imply a better prognosis and reduced chance of developing other liver diseases.

This study observed a significant reduction in the levels of liver enzymes, which were close to being normalized, among the 4 patients with chronic hepatitis B abnormal liver function after receiving ABM extract for 12 months. For cases 1, 2, and 4, the levels of aspartate aminotransferase and alanine aminotransferase were found to decrease with time. For case 3, who suffers from chronic hepatitis B and C, the levels of aspartate aminotransferase and alanine

aminotransferase decreased after 9 months of ABM treatment. This can be attributed to his liver disease being more serious and complicated. Symptoms of malaise, poor appetite, and abdominal fullness in case 4 improved soon after the patient took the extract of ABM. Since there were no adverse side-effects or discomfort reported during the study period, we can consider the ABM extract safe for taking as a supplement.

Our previous study has demonstrated the benefits of ABM extract as a supplement for reducing the homeostasis model assessment for insulin resistance in subjects with type 2 diabetes treated with gliclazide and metformin.[5] Rich polysaccharides such as β-glucans are found to be the main compounds of ABM.[8,10] β-Glucans from ABM have demonstrated antidiabetic activity.[10] Thiazolidinediones have been found to improve peripheral insulin resistance and have been employed for treating type 2 diabetes.[11,12] However, some adverse side-effects on liver function have also been reported.[12] Hence, ABM can be a possible supplement for type 2 diabetes with hepatitis B and abnormal liver function.

Use of complementary medicine has been common among patients with hepatitis B. There is a tradition in Chinese medicine of using the fungus ABM as a medicine.[13] The ABM extract was obtained from dried fungal bodies of ABM, which has been widely taken as a health care product in Taiwan and Japan for years.[5,13] ABM is rich in polysaccharide, which vitalizes production of interferon and interleukin that prevent viruses from entering the tissue.[7] The benefit of ABM on hepatitis B has been demonstrated in an *in vivo* study.[6] The potential beneficial effects of AMB for patients with chronic hepatitis B are worth further exploration in detailed clinical studies.

Despite the encouraging results, our work still had limitations, such as the absence of controls and a small study sample. In fact, this is only an initial clinical observation. Future research should be performed with well-designed protocols.

In conclusion, our initial observation seems to indicate the potential benefits of ABM extract in normalizing liver function of patients with chronic hepatitis B. Controlled studies with large samples should be conducted in the future.

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The Mushroom *Agaricus blazei* Murill in Combination with Metformin and Gliclazide Improves Insulin Resistance in Type 2 Diabetes: A Randomized, Double-Blinded, and Placebo-Controlled Clinical Trial

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Background: Complementary and alternative medicine use in adults with type 2 diabetes is popular. Although most of the herbs and supplements appear to be safe, there is still insufficient evidence that demonstrates their definitive beneficial effects. This study was done to determine whether the supplement of *Agaricus blazei* Murill extract improves insulin resistance in type 2 diabetes.

Materials and Methods: This study was a clinical randomized, double-blind, placebo-controlled trial. Of a population of 536 registered diabetes patients with 72 subjects (1) aged between 20 and 75 years, (2) being Chinese, (3) having type 2 diabetes for more than 1 year, and (4) having been taking gliclazide and metformin for more than 6 months were enrolled in this study. The enrolled patients were randomly assigned to either receiving supplement of *Agaricus blazei* Murill (ABM) extract or placebo (cellulose) 1500 mg daily for 12 weeks. Homeostasis model assessment for insulin resistance (HOMA-IR) was used as the major outcome measurement.

Results: At the end of the study, subjects who received supplement of ABM extract ($n = 29$) showed significantly lower HOMA-IR index (3.6[standard deviation, 2.5] versus 6.6[standard deviation, 7.4], $p = 0.04$) than the control group ($n = 31$). The plasma adiponectin concentration increased 20.0(standard deviation, 40.7)% in the ABM group after 12 weeks of treatment, but decreased 12.0(20.0)% among those taking the placebo ($p < 0.001$).

Conclusions: Supplement of ABM extract improves insulin resistance among subjects with type 2 diabetes. The increase in adiponectin concentration after taking AMB extract for 12 weeks might be the mechanism that brings the beneficial effect. Studies with longer periods of follow-up should be conducted in the future.

INTRODUCTION

Type 2 diabetes represents a heterogeneous group of disorders characterized by increased insulin resistance.[1] Lifestyle, diet, obesity, and family history of diabetes have been associated with the development of insulin resistance, although the molecular pathway remains unknown.[2] Thiazolidinediones (TZD) have been found to improve peripheral insulin resistance and has been employed for treating type 2 diabetes.[3,4] However, some adverse side effects on liver function have also been reported.[5] Hence, it is desirable to find a natural herbal medicine that can help boost insulin resistance but has less undesirable side effects.

The mushroom *Agaricus blazei* Murill (ABM) is a natural food, which has been used as a health care product for the prevention of a range of illness including cancer, diabetes, arteriosclerosis, and chronic hepatitis. It has been reported that ABM has beneficial effects in fighting cancer,[6–10] virus,[11] and *Streptococcus* pneumonia infection in mice[12] as well as enhancing antibody production of vaccine.[13,14] Rich polysaccharides such as β-glucans are found to be the main compounds of ABM.[14–17] β-Glucans from

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ABM have demonstrated antidiabetic activity.[17] An animal model study and a pilot study have both indicated its beneficial effect in type 2 diabetes. Hence, we conducted this clinical trial to examine whether ABM extract given as a supplement can improve insulin resistance in type 2 diabetes.

RESEARCH DESIGN AND METHODS

Study population

The trial was conducted from July 1, 2005 through December 31, 2005 in the Taipei Hospital, Taiwan. Of a population of 536 registered patients with diabetes, 72 subjects met with the inclusion criteria: (1) aged between 20 and 75 years; (2) being Chinese; (3) having type 2 diabetes for more than 1 year; and (4) having been taking gliclazide and metformin for more than 6 months were enrolled in this study; and exclusion criteria were as follows: (1) aminotransferases aspartate or aminotransferases alanine >80 IU/L, serum creatinine >2.0 mg/dL; (2) prolacting or pregnant women, heart failure, acute myocardic infarct, stroke, and heavy injuries; and (3) any other conditions not suitable for trial as evaluated by the physician.. The protocol was approved by the Human Ethics Committee of our hospital. Informed consent was obtained from all the enrolled patients. The patients were instructed to maintain an isocaloric diet and their previous eating habits during the study period. All subjects were free to withdraw at any time during the course of the study.

Preparation of sample and treatment

ABM is a health care product popularly used in Taiwan. Our ABM extract samples, obtained from Eng Chiao Bio-Technology Co. Ltd., Taiwan, were extracted from dried fungal bodies of ABM according to the preset standard procedures with certificate of analysis given. The placebo given to the control group comprised pure microcrystalline cellulose. The subjects were asked to take one capsule containing 500 mg of either ABM extract or cellulose three times each day for 12 weeks. The capsule was taken with gliclazide 30 minutes before eating and metformin was taken 30 minutes after eating. During the study period, the subjects should keep taking the same dose of gliclazide and metformin except when hypoglycemia occurs, in which case the dose of gliclazide or metformin should be reduced immediately.

Randomization and blindness

All subjects were randomly assigned to one of the two groups. A random number between 0.0 and 0.99 would be generated by the computer for each patient. Patients with a random number between 0.0 and 0.49 were assigned to the group with ABM extract given, whereas those with a random number between 0.50 and 0.99 would be assigned to the placebo group with cellulose given. The same opaque capsules containing either dried powdered ABM extract or placebo (cellulose) were administered to the subjects by a research assistant blinded to the contents in the capsules. All patients were treated in the same fashion.

Assessment

Homeostasis model assessment for insulin resistance (HOMA-IR) [fasting glucose (mmol/L) × fasting insulin (UI/L)/22.5] was used as the major outcome measurement.[18,19] At baseline and after 12 weeks of treatment, anthropometric measurements, blood pressure, fasting glucose, hemoglobulin A1C% (HbA1C), insulin, adiponectin and plasma lipoproteins (triglyceride, cholesterol, cholesterol–high-density lipoprotein, and cholesterol–low-density lipoprotein) of both groups were measured. The change (%) in concentration of adiponectin after the 12-week treatment was also evaluated.

All measurements were made at 8 AM to 9 AM after an overnight fast using standardized methods. A sample of whole blood was drawn and centrifuged at 4°C, and a 1-mL aliquot of serum was rapidly frozen (−80°C) for subsequent hormone analysis. The plasma adiponectin concentration was measured by a radioimmunoassay kit (Linco Research, Inc., St. Charles, Missouri). This kit employs the double-antibody/polyethylene glycol technique using ^{125}I-lableled adiponectin and a multispecies adiponectin rabbit antiserium. Plasma insulin levels were measured using a commercially available radioimmunoassay (Linco Research Inc.). The intra- and interassay coefficients of variation were 3.1% and 4.9%, respectively. The limit of sensitivity is 0.5 ng/mL.

Statistical analysis

The data were analyzed with SPSS software (version 11.5, SPSS Software, Inc., Chicago, IL). Paired t tests were used to examine differences within-group at 0 to 12 weeks. Student t test was used to examine the main outcome, demographic data, and other measurements between group means. Chi-square test was employed for gender comparison between groups. All p values were two-tailed, and the α level of significance was set at 0.05. We estimated in power 0.8 that each group required 28 subjects.

RESULTS

Demographics

Seven subjects of the ABM extract group and five subjects of the placebo group withdrew because of personal reasons. In the end, 60 patients completed the study. Table 1 shows the demographic data, fasting serum glucose meta-

TABLE 1. CHARACTERISTICS OF SUBJECTS AT BASELINE

	Agaricus blazei *Murill extract* (n = 29)	*Placebo control (cellulose)* (n = 31)	p *value*
Basic data			
Gender (male/female)	14/15	13/18	0.41
Age (years)	57.0 (9.4)	56.4 (12.0)	0.83
Time since diagnosis of diabetes (y)	57.0 (9.4)	56.4 (12.0)	0.83
Daily dose of gliclazide (mg)	9.1 (7.5)	8.2 (6.6)	0.65
Daily dose of metformin (mg)	171.0 (28.1)	175.5 (43.4)	0.64
Body mass index (kg/m^2)	1658.6 (557.3)	1690.3 (646.7)	0.84
Waist circumflex (cm)	25.5 (3.1)	27.4 (5.7)	0.11
Systolic blood pressure (mm Hg)	131.3 (16.7)	138.9 (14.8)	0.08
Diastolic blood pressure (mm Hg)	78.3 (10.6)	82.8 (9.8)	0.10
Fasting serum glucose metabolic factors			
Glucose (mg/dL)	181.0 (66.9)	194.6 (57.6)	0.40
HbA1c (%)	8.9 (1.3)	9.1 (1.5)	0.55
Insulin (UI/L)	10.6 (6.6)	12.8 (17.8)	0.55
HOMA-IR index	4.8 (3.5)	6.3 (9.2)	0.40
Adiponectin (ng/mL)	15.8 (7.3)	18.4 (7.8)	0.20
Plasma lipoprotein			
Fasting triglyceride (mg/dL)	160.5 (114.4)	229.6 (224.3)	0.14
Fasting cholesterol (mg/dL)	181.3 (42.5)	187.5 (50.2)	0.61
HDL-cholesterol (mg/dL)	43.9 (7.3)	42.7 (8.7)	0.58
LDL-cholesterol (mg/dL)	116.6 (38.2)	107.0 (38.1)	0.51
Other fasting serum factors			
Aminotransferases, aspartate (IU/L)	32.4 (19.7)	29.5 (15.6)	0.53
Aminotransferases, alanine (IU/L)	24.5 (11.6)	24.5 (10.2)	1.0
Creatinine (mg/dL)	0.9 (0.2)	1.0 (0.2)	0.08

HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment for insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

bolic factors, plasma lipoprotein, and clinical profiles of the groups at the time of entry. As can be seen, there were no significant differences in all the baseline measurements between the ABM extract group and the placebo group.

Within-group comparison at 12 weeks

Table 2 shows the within-group comparisons at baseline and after the 12-week treatment. According to the analysis of the fasting serum glucose metabolic factors, the ABM extract group showed a significant difference in reduced HbA1C, insulin concentration, and homeostasis model assessment for insulin resistance (HOMA-IR) index as well as increased concentration of adiponectin, compared with the initial values, whereas the placebo group showed significant difference only in reduced adiponectin level compared with the initial values.

Between-group comparison at 12 weeks

At the end of 12 weeks (Table 2), there were no significant differences between the two groups in all the measurements except insulin concentration and HOMA-IR index ($p = 0.05$ and 0.04). Figure 1 shows a significant difference between the ABM extract group and the placebo group ($p < 0.001$) in terms of change (%) in plasma adiponectin concentrations after 12 weeks of treatment.

Adverse effects

Three subjects of the ABM extract group had hypoglycemia-like symptoms; 2 patients had the dose of oral hypoglycemia agent (OHA) reduced, whereas 1 patient withdrew. One subject of the placebo group also developed hypoglycemia-like symptoms. The dose of OHA was reduced and he stayed on in the study.

Two subjects of the ABM extract group developed skin itching, 1 subject of the placebo group had skin allergy with papules, and another had nausea and fullness sensation. All 4 of them withdrew. No major adverse effects were noticed.

DISCUSSION

This study shows the benefits of ABM extract supplement for reducing the HOMA-IR index in subjects with type 2 diabetes treated with gliclazide and metformin.

Insulin resistance, a common cause of type 2 diabetes, implies impairment of insulin signaling in target tissues. It has been reported that some OHA might influence insulin resistance.[4,5,17,20–22] To avoid existing confounders and bias, we examined a homogenous Chinese cohort who had had type 2 diabetes for more than 1 year and had been taking gliclazide and metformin for more than 6 months.

TABLE 2. CHARACTERISTICS OF SUBJECTS AFTER 12-WEEK TREATMENT

	Agaricus blazei *Murill extract* (n = 29)	*Placebo control (cellulose)* (n = 31)	p *value*
Basic data			
Daily dose of gliclazide (mg)	168.3 (32.7)	175.5 (43.4)	0.47
Daily dose of metformin (mg)	1634.9 (570.4)	1706.5 (635.1)	0.65
Body mass index (kg/m^2)	25.6 (3.0)	27.7 (5.7)	0.08
Waist circumflex (cm)	88.0 (8.4)	92.9 (14.0)	0.11
Systolic blood pressure (mm Hg)	131.2 (16.5)	139.7 (15.4)	0.06
Diastolic blood pressure (mm Hg)	77.2 (10.8)	83.2 (10.4)	0.07
Fasting serum glucose metabolic factors			
Glucose (mg/dL)	182.3 (52.9)	197.9 (55.9)	0.27
HbA1c (%)	8.3 (1.8)*	8.9 (1.7)	0.24
Insulin (UI/L)	7.8 (4.9)*	13.5 (7.8)	0.05
HOMA-IR index	3.6 (2.5)*	6.6 (7.4)	0.04
Adiponectin (ng/mL)	18.8 (10.9)*	16.3 (8.3)*	0.33
Plasma lipoprotein			
Fasting triglyceride (mg/dL)	141.8 (73.5)	215.5 (207.3)	0.07
Fasting cholesterol (mg/dL)	200.5 (44.7)	192.7 (31.0)	0.44
HDL-cholesterol (mg/dL)	44.4 (7.1)	41.8 (8.8)	0.22
LDL-cholesterol (mg/dL)	136.4 (46.8)	121.1 (34.8)	0.16
Other fasting serum factors			
Aminotransferases, aspartate (IU/L)	31.4 (23.4)	31.5 (15.3)	0.99
Aminotransferases, alanine (IU/L)	24.0 (10.9)	26.9 (14.0)	0.37
Creatinine (mg/dL)	0.9 (0.2)	1.0 (0.2)	0.09

Data are means (SD).

*$p < 0.05$ from baseline to the end (12 weeks) with paired t tests.

HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment for insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

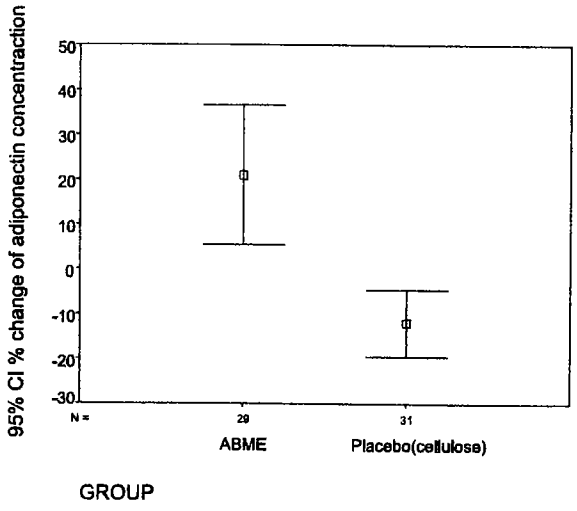

FIG. 1. Change (%) in plasma adiponectin concentrations after 12-week treatment in *Agaricus blazei* Murill extract (ABME) group and placebo (cellulose) group ($p < 0.001$). CI, confidence interval.

Many animal model studies have demonstrated the antidiabetic activity of ABM.[17] After an animal model study in 2003 and a pilot study had showed its beneficial effect in patients with type 2 diabetes, we conducted this clinical trial to examine whether the supplement of ABM extract improves insulin resistance in patients with type 2 diabetes. We also evaluated the adiponectin concentration using many fasting serum glucose metabolic factors to further examine the possible mechanism of its beneficial effects.

In this study, subjects who received the supplement of ABM extract showed a significant reduction in HOMA-IR index (from 4.8 to 3.6), which was much lower than that observed among the control subjects (from 6.3 to 6.6).

It is interesting to note that the subjects who had taken a supplement of ABM extract for 12 weeks showed a significant increase in plasma adiponectin concentrations compared with the placebo (cellulose) group ($p < 0.001$) (Fig. 1). Many previous studies have reported that the adiponectin level might be a major modulator of insulin resistance[23] and predict the development of type 2 diabetes.[24–26] Circulating adiponectin levels in human is positively correlated with insulin sensitivity.[23,27] The level of adiponectin appeared to play a very important role in the regulation of insulin acting and energy homeostasis.[27,28] We observed a 20% increase in adiponectin level after 12 weeks of treatment with

ABM extract supplement. This might account for the effect of improving insulin resistance in the ABM extract group.

Our finding reveals that after the 12-week treatment, subjects receiving ABM extract had a 6.7% reduction of HbA1C (from 8.9 to 8.3) and those taking cellulose had a 2.4% reduction (from 9.1 to 8.9). Although both supplements showed a similar effect on reducing HbA1C with no statistical difference, the results still had clinical implications. In the AMB extract group, the decrease in HbA1C could be attributed to the improved insulin resistance, whereas that in the control group might be caused by loss of appetite or reduced food intake. Although the initial results showed no statistical difference in HbA1C, treatment of longer duration might result in significant statistical difference.

As mentioned in our study design, all the subjects should maintain the same dose of gliclazide and metformin during the study period unless hypoglycemia occurs. During the 12-week treatment, 3 subjects of the ABM extract group developed hypoglycemia-like symptoms; 2 patients had the dose of OHA reduced and stayed in the study whereas the other patient withdrew. Although at the end of study there was no significant difference in the dose of OHA received, the supplement of ABM extract might have the effect of reducing the current OHA dose for type 2 diabetes, which is beneficial to diabetes control. Hence, future studies on effects of ABM should be alert for hypoglycemia-like symptoms.

Although many positive effects of ABM have been reported, most of them were from *in vitro* or animal studies.[6–17] To our knowledge, this is the first randomized clinical ABM study. Our results reveal improvement in insulin resistance by ABM. Although TZD can enhance insulin sensitivity,[3,4,29] its toxicity affects the liver.[5] Hence, ABM can be a possible supplement that has no major adverse effects and does not result in liver function impairment, as noted in this study. Attention must be paid to the 2 subjects of the ABM extract group who developed skin itching. Clinical observation of other possible side effects should be made in future.

Complementary and alternative medicine use in adults with type 2 diabetes is popular.[30–32] Although most of the herbs and supplements appear to be safe, there is still insufficient evidence that demonstrates their definitive beneficial effects.[31] The ABM extract was obtained from dried fungal bodies of ABM, which has been widely taken as a health care product in Taiwan and Japan for years. The effect of insulin resistance improvement attributed to taking supplement of ABM extract was demonstrated in our studies. The beneficial effects of AMB are worth further exploration in detailed clinical studies.

Despite the encouraging results, our work still had limitations, such as short period of study. Future research should be performed with a longer follow-up period and other well-designed protocols.

In conclusion, this study demonstrated that supplementation with ABM extract improves insulin resistance in type 2 diabetes. The increase in adiponectin concentration after 12-week treatment with ABM extract supplement might be the mechanism that brings beneficial effect. Studies with a longer period of follow-up should be made in the future.

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Measuring perceived effects of drinking an extract of basidiomycetes *Agaricus blazei* murill: a survey of Japanese consumers with cancer

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Abstract

Background: To survey cancer patients who consume an extract of the Basidiomycetes *Agaricus blazei* Murill mushroom (Sen-Sei-Ro) to measure their self-assessment of its effects and to develop an instrument for use in future randomized trials.

Methods: We designed, translated and mailed a survey to 2,346 Japanese consumers of Sen-Sei-Ro self-designated as cancer patients. The survey assessed consumer demographics, cancer history, Sen-Sei-Ro consumption, and its perceived effects. We performed exploratory psychometric analyses to identify distinct, multi-item scales that could summarize perceptions of effects.

Results: We received completed questionnaires from 782 (33%) of the sampled Sen-Sei-Ro consumers with a cancer history. Respondents represented a broad range of cancer patients familiar with Sen-Sei-Ro. Nearly all had begun consumption after their cancer diagnosis. These consumers expressed consistently positive views, though not extremely so, with more benefit reported for more abstract benefits such as emotional and physical well-being than relief of specific symptoms. We identified two conceptually and empirically distinct and internally consistent summary scales measuring Sen-Sei-Ro consumers' perceptions of its effects, Relief of Symptoms and Functional Well-being (Cronbach's alpha: Relief of Symptoms, $\alpha = .74$; Functional Well-Being, $\alpha = .91$).

Conclusion: Respondents to our survey of Sen-Sei-Ro consumers with cancer reported favorable perceived effects from its use. Our instrument, when further validated, may be a useful outcome in trials assessing this and other complementary and alternative medicine (CAM) substances in cancer patients.

Background

Complementary and alternative medicine (CAM) is widely used by patients who are undergoing or have completed medical treatment for cancer [1,2]. While conventional therapies, including surgery, radiation therapies and anticancer drugs, are targeted at tumors, their side

effects on normal organs may significantly compromise quality of life during and after treatment. For many patients, CAM approaches may be pursued in order to augment conventional modalities' anti-cancer effects, as well as to reduce treatment-related symptoms and other side effects that diminish their quality of life [3-5]. While the distinction between biological end points and the broader perspective of outcomes research is important to any assessment of oncology practice [6], it is particularly important when patients use CAM therapy for these less clearly defined objectives. However, few investigations have attempted to measure rigorously the goals patients have in using these substances and whether they achieve them. We have learned that measuring quality of life outcomes in cancer patients in ways that accurately reflect their perspectives is challenging [7-9]. We found an opportunity to address this challenge when asked to design a survey of Japanese users of a widely used CAM substance, Sen-Sei-Ro.

Sen-Sei-Ro is an extract derived from mushroom, Basidiomycetes *Agaricus blazei* Murill, that has been reported to have a stable antioxidant activity [10], as well as antimutagenic [11,12], antitumorigenic [13-16], chemopreventive [17] and immunostimulatory effects [17,18], and improved quality of life associated with immunological effects in a cohort of cancer patients [19]. In addition, a study of the 12,465 residents of Nagano Prefecture of Japan found lower cancer death rates among mushroom farmers compared to other residents of the prefecture [17]. Sen-Sei-Ro has been manufactured and marketed in Japan by Kyowa-S.S.I. since 1991 and, according to company estimates, has been purchased by as many as 700,000 cancer patients. In previous surveys of its consumers the company has found that improved quality of life was an important rationale for Sen-Sei-Ro consumption. We constructed a survey of Sen-Sei-Ro consumers with cancer to identify patients' demographic and medical characteristics, patterns of use, perceived benefits and rationale for use of this product. We also hoped to identify domains of interest for a patient-reported measure to be used in a controlled clinical trial of its effects on quality of life of cancer patients. Such an instrument, once validated, could also be applied more broadly to measuring the impact of other CAM products taken by cancer patients for purposes other than specific anti-tumor effects.

Methods

A total of 2,346 Japanese consumers of Sen-Sei-Ro, listed in the Kyowa-S.S.I. database, were mailed a brief questionnaire in July 2001. Using a common industry practice of including questionnaires as product package inserts, the company had surveyed the consumption habits and health status of Sen-Sei-Ro consumers in 2000. Consumers who indicated they had cancer were eligible for the present survey. We developed a draft survey instrument in English, which was translated into Japanese and then back-translated into English to confirm the preservation of item definitions. A subsequent round of revisions was made. The instrument was mailed to current customers who in the previous survey had indicated that they either had been treated for cancer or used the product to mitigate the effects of cancer or cancer treatment.

The questionnaire included 37 items that assessed demographics (i.e., gender, age, and marital status), cancer history, consumption of Sen-Sei-Ro, and its perceived effects. Cancer status included questions about the primary tumor (i.e., 'Where did your cancer start?") and current treatment with intravenous chemotherapy, oral chemotherapy or radiation. It assessed consumption by asking when its use began relative to the cancer diagnosis and treatment and the amount and duration of use. Seven questions asked about the extent to which drinking Sen-Sei-Ro helps to: strengthen one's body so it can fight cancer and resist other illnesses, reduce symptoms of cancer and the side effects of treatment, cure cancer, feel better emotionally, and engage cancer spiritually. Finally, two items assessed motives for use: the importance of one's own efforts in fighting cancer, relative to "what doctors do," and family support for the notion that drinking it "will help me fight cancer."

Respondents' perceptions of more specific effects on quality of life were assessed by asking about 17 changes they may have noticed "about your body, how you feel physically, and how you feel emotionally" since they had been taking Sen-Sei-Ro. Response options included "better," "worse," and "about the same." These items were based on the previous survey, the clinical experiences of physicians in Korea who used it as part of their cancer patients' care [19], and our previous experience in assessing quality of life in cancer patients. The items were designed to assess a broad array of treatment side effects and aspects of physical function and emotional well being.

The analysis was designed to describe consumers' perceptions of the quality of life effects of using Sen-Sei-Ro and explore variation in their perceptions with respect to demographic and medical characteristics and product usage. In order to examine patterns in perceptions of the effects we conducted a principal components factor analysis with orthogonal rotation with the 17 individual effects items. Each item was coded so that increasing values indicated greater relief from symptoms. The factor results were then used to explore the definition of distinct, multi-item scales that could summarize perceptions of effects. Following psychometric convention, the Likert response set was considered and analyzed as an interval scale [20,21]. Such scales would offer increased overall

reliability compared to reporting multiple individual items, as well as allow a more parsimonious description of the effects respondents attribute to using Sen-Sei-Ro. Associations between scale scores and ordered and nonordered categorical indicators of consumer characteristics and product usage were evaluated by calculating Spearman correlation coefficients, t-tests, and analyses of variance, as appropriate.

Results

We received completed questionnaires from 782 (33%) of the sampled Sen-Sei-Ro consumers with a history of cancer. The respondents represented a broad range of cancer patients familiar with both cancer treatment and Sen-Sei-Ro. Slightly more than half were male (53%), 89% were married, and the median age was 65, with 87% between 51 and 80 years old (range: 31–91). Most respondents reported a single cancer, but 19% reported two or more (Table 1). Lung, colon and gastric cancer patients each accounted for one-fifth of diagnoses. However, patients with cancers that only or disproportionately affect women (uterus, cervix, and breast) outnumbered those with diagnoses confined to men (prostate), 191 (24%) vs. 75 (10%). Although most of these study participants were currently receiving cancer therapy, 37% were not, and 23% were receiving oral chemotherapy, radiation or both, and 39% were receiving intravenous chemotherapy, which is usually more toxic.

Over 90% of the respondents had used the product for over 3 months, and over half for more than a year (Table 2). Only 3% of the study participants began using it before cancer was diagnosed, while approximately one-third initiated use after diagnosis, another third after treatment began and the remaining patients after treatment was completed. Nearly all used it daily, and 42% drank more than one pack each day.

Table 1: Clinical Characteristics of 782 Consumers of Sen-Sei-Ro Who Responded to a Survey

Characteristic	Number	Percent
Number of cancers reported		
One	632	80.6
Two	129	16.5
Three or more	21	2.7
Where cancer(s) started		
Lung	177	23
Colon	170	22
Stomach	158	20
Liver	127	16
Breast	101	13
Ovaries	40	5
Cervix	29	4
Uterus	21	3
Prostate	75	10
Others (name of the organ or a part of body)	62	8
Current treatment		
No active treatment	292	37.4
Receiving oral chemotherapy or radiation only	181	23.2
Receiving intravenous chemotherapy?	307	39.4

These study participants expressed consistently positive views, though not extremely so, regarding general benefits. Between 62 and 74% said Sen-Sei-Ro helps in various respects, such as improving strength to fight cancer and ameliorating the side effects of treatment (Table 3). However, only 16% indicated it was a "great help" in building resistance to illnesses other than cancer, while 31% strongly endorsed its value in helping spiritually to fight cancer. The study participants endorsed two indicators of motivations for using it. Nearly all (93%) agreed, and a majority (51%) strongly, that relying on doctors alone is insufficient, implying they may believe that using Sen-Sei-Ro represents an important additional personal effort. Nearly all study participants (85%) also agreed that their families think it helps fight the cancer. Although the family's reported endorsement of this belief was somewhat weaker than the consumer's personal endorsement, virtually no one rejected it.

Positive and negative effects of Sen-Sei-Ro

The factor analysis of the 17 individual perceived effects items suggested two distinct constructs: Relief of Symptoms and Functional Well-being. The first referred to relief of specific symptoms and was defined by items pertaining to likely side effects of cancer and its treatment (e.g., appetite, weight loss, pain, nausea). The second factor was defined by perceptions of effects on strength, vitality, and emotional well-being. Subsequent evaluation of scales defined by these two sets of items, including item-scale discrimination and internal consistency, identified two items pertaining to effects on sleep and daytime drowsiness that discriminate poorly. That is, they were equally correlated with both scales, and thus were deleted. The remaining items displayed clear discrimination, correlating highly with their assigned scale and little with the other. As a result, we defined two conceptually and empirically distinct, and internally consistent (Cronbach's alpha: Relief of Symptoms, α = .74; Functional Well-Being, α = .91) summary scales of Sen-Sei-Ro study participants' perceptions of its effects relative to their cancer treatment. We present the useful items remaining after this analysis in Table 4. Scores were calculated by averaging the scores of the constituent items, and thus ranged from -1 to +1, with 0 indicating a perceived effect that was neither positive nor negative.

Scale scores indicate that study participants reported generally favorable effects as indicated by the positive mean scores, although the majority of patients reported no

Table 2: History of Use of Sen-Sei-Ro Reported by 782 Survey Respondents

Characteristic	Number	Percent
How long have you been taking "Sen-Sei-Ro?	(median: more than a year)	
Less than a month	9	1.2
1–3 months	57	7.3
3–6 months	108	13.9
6 months- 1 year	172	22.1
More than 1 year	432	55.5
When did you start drinking "Sen-Sei-Ro?"	(median: after starting treatment)	
Before the cancer diagnosis	22	2.9
At the time of cancer diagnosis (before surgery or chemotherapy)	218	28.4
After starting the treatment (surgery or chemotherapy)	266	34
After completion of treatment (surgery or chemotherapy)	262	34.1
What best describes your situation?	(median: every day)	
Drink it every day (routinely)	644	84.4
Drink while I am undergoing cancer treatment	71	9.3
Drink when I am feeling poorly, tired, and weak)	22	2.9
Drink when I am feeling worried about my cancer)	26	3.4
How many packs do you drink, on the average, per week?	(median: 1 pack/day)	
Less than 7 packs (less than 1/day)	49	6.4
7 packs (1 pack/day)	369	48.4
2 packs/day	195	25.6
3 packs/day	126	16.5
4 or more packs/day	24	3.1

effect either way on most individual items, and net scores of zero were reported by 26% and 37% for Functional Well-Being and Relief of Symptoms, respectively. The product was perceived to be somewhat more effective in promoting overall well-being (mean = .34, sd = .46) than in relieving symptoms (mean = .25, sd = .36). The most frequently reported specific benefits were for emotional (spiritual) well-being (50%), physical well-being (50%), energy level (44%), and strength (41%), with far fewer reporting benefit for specific muscle weakness. Large minorities (30% or more) felt it helped with anxiety or sadness, depression, daily activities and socializing with others. While Sen-Sei-Ro was less frequently seen as effective in alleviating common symptoms that are side effects of conventional treatment, a third or more reported bene-

Table 3: Perceived Help from Sen-Sei-Ro by 782 Survey Respondents

	Percent		
How much do you think that drinking "Sen-Sei-Ro" helps with the following?	No help	Help	Great help
A. Improves my body strength to fight cancer	5	70	25
B. Improves my resistance against sickness other than cancer	10	74	16
C. Helps reduce symptoms of cancer	10	65	24
D. Helps reduce the side effects of cancer therapy	12	67	21
E. Helps with cancer treatment	10	67	24
F. Helps with improving emotional condition	9	66	25
G. Helps me spiritually to fight against cancer	6	62	31

Table 4: Summary Scales of Noticed Effects of Using Sen-Sei-Ro From 782 Respondents

	Treatment Symptoms	**Functional Well-being**
	Item-Scale Correlations[1]	
Appetite	**0.50**	0.44
Maintained or gained weight	**0.53**	0.37
Lost weight	**0.48**	0.39
Feelings of pain	**0.54**	0.36
Ability to reduce hair loss or grow hair	**0.36**	0.28
Nausea or vomiting	**0.44**	0.38
Muscle weakness	0.39	**0.51**
Energy level	0.43	**0.75**
Physical strength	0.44	**0.73**
Feelings of tension, worry	0.38	**0.72**
Feelings of sadness, depression	0.43	**0.65**
Ability to spend time with other people	0.41	**0.70**
Ability to work or get chores done around the house	0.46	**0.75**
Overall sense of physical well being	0.50	**0.75**
Overall sense of emotional well being	0.39	**0.70**
Cronbach alpha	0.74	0.91

[1] Item-scale correlations, shown in bold face, are corrected of overlap. Items included in factor analysis, but deleted from summary scales because of poor scale discrimination include: falling asleep quickly; feeling sleepy during the day;

fits with respect to appetite and maintenance of body weight. More than 1 in 5 felt it helped with sleeplessness, pain and hair loss.

Perceived effects of using it were associated with gender, age, and tumor site. Women and those with uterine cancers reported better Functional Well-Being, but parallel trends for Relief of Symptoms did not achieve statistical significance (Table 5). Younger patients tended to report more positive effects on Functional Well-Being, but not on Relief of Symptoms. Surprisingly, current active anticancer treatment did not affect either scale, although patients who began using the product earlier in their course tended to report more benefit on Relief of Symptoms. The amount consumed each week was not associated with perceived effects in either domain (data not shown).

Study participants with aggressively treated, poor prognosis cancers (lung, gastric and liver) tended to report less

Table 5: Perceived Effects Scale Scores by Characteristics of 782 Respondents

		Relief of Treatment Symptoms	test of association (p value)	Improve Functional Well-being	test of association (p value)
			(mean scores)		
All Respondents		0.25		0.30	
Percent reporting no net effect		26%		37%	
Sex					
Male		0.23	t	0.25	t
Female		0.27	(0.092)	0.36	(< 0.001)
Age group					
20 – 49		0.30		0.42	
50 – 59		0.27	r = -0.03	0.29	r = -0.08
60 – 69		0.23	(0.389)	0.30	(0.016)
70 and older		0.25		0.26	
Cancer group					
Lung, stomach, liver		0.23	F	0.28	F
Colon, breast, uterus, cervix		0.29	(0.060)	0.35	(0.004)
Prostate, other		0.21		0.15	
Lung	No	0.27	t	0.32	t
	Yes	0.20	(0.032)	0.26	(0.190)
Stomach	No	0.25	t	0.29	t
	Yes	0.27	(0.379)	0.34	(0.245)
Liver	No	0.26	t	0.31	t
	Yes	0.18	(0.026)	0.23	(0.059)
Colon	No	0.24	t	0.29	t
	Yes	0.29	(0.074)	0.33	(0.295)
Breast	No	0.25	t	0.29	t
	Yes	0.26	(0.725)	0.36	(0.192)
Uterus	No	0.25	t	0.29	t
	Yes	0.39	(0.075)	0.50	(0.051)
Cervix	No	0.25	t	0.30	t
	Yes	0.26	(0.836)	0.42	(0.159)
Prostate	No	0.25	t	0.32	t
	Yes	0.21	(0.277)	0.14	(0.002)
History using sen-sei-ro					
≤ 3 months		0.14*		0.22	
3 – 6 months		0.24	r(s) = 0.07	0.30	r(s) = 0.04
6 – 12 months		0.25	(0.059)	0.29	(0.251)
> 12 months		0.27		0.32	
Current treatment					
No active treatment		0.24	F	0.31	F
Oral or radiation therapy		0.26	0.640	0.30	0.973
Intravenous chemotherapy		0.26		0.30	

t: t-test.
F: F, analysis of variance.
r: Pearson correlation coefficient; r(s): Spearman correlation coefficient.
* Group mean is significantly ($p < 0.05$) lower than means for other groups, which are not significantly different from one another

benefit than those with less aggressively treated cancers (colon, breast, uterus or cervix). Those with prostate cancer and other cancers that seldom received chemotherapy during the survey period reported the least benefit.

Discussion

This survey of consumers of Sen-Sei-Ro who reported a history of cancer found that nearly all began using it after their cancer was diagnosed, and those who started using it earlier in their cancer course tended to report greater benefit. Most patients report benefit from consuming this product and large proportions feel using it is a "great help." A survey of people currently using the product by choice produces a bias toward reported benefit, which our results reflect, and the relatively low 33% survey response rate probably increases the bias. However, despite the evident predisposition in favor of the product and the generally positive reports for more global benefits from its use, most of these study participants report little substantial effect in either direction when queried about specific consequences of cancer or its treatment.

Our findings shed some light on these patients and our measures. Our factor analysis of items focusing on 17 more or less specific effects indicated two major constructs that characterize study participants' perceptions of potential benefits of using Sen-Sei-Ro: relief of cancer and treatment-related symptoms and improvement in overall functional status and well-being, which fits with previous studies of cancer patients' motivations for pursuing CAM [4,22,23]. Like others, we found that improvements in functional well-being were greater than relief of symptoms, suggesting that cancer patients use CAM products for their effects, rather like a health promoting tonic, in strengthening their body's ability to recover from the debility of cancer treatment and support its ability to fight against cancer [22,24,25]. Our results provide some additional evidence of the validity of these measures. Younger patients, women, study participants with longer usage and thus more time to recover from initial cancer treatments, and those whose cancers had less poor prognoses and less aggressive treatment are all generally less symptomatic and in better overall health, and all tended to report more benefit by both measures. These results are consistent with both patients' limited understanding of pathophysiology and the sensitivity of these scales to their true condition: they felt better and thus able to ascribe benefit to Sen-Sei-Ro than others expected to be worse off. The still lower benefit reported by prostate cancer patients may reflect their better overall well-being and few symptoms from disease or treatment, providing little potential for benefit from Sen-Sei-Ro. The 2 scales postulated here appear sensitive to patient changes in two domains relevant to CAM use and may prove useful as outcome measures in future controlled trials of these substances in cancer patients.

Previous studies have helped to characterize who is likely to use dietary supplements, such as Sen-Sei-Ro and complementary and alternative medicine products more broadly. In studies of cancer patients and other populations in North America and Europe, the probability of choosing these approaches is greater with female gender, older age, higher education, lower body mass and indicators of healthy lifestyles, such as frequent exercise, avoidance of smoking, and diets low in fat and high in fruits and vegetables [26-32]. In a large national study in Japan, Ishihara et al. reported that 11% of men and 16% of women used dietary supplements, with use associated with older age, lower body mass, and frequent exercise, as well as longer work days (for men), and greater stress [32]. The reasons cancer patients give for using dietary supplements appear to revolve around three main themes, characterized in one study as surviving cancer (i.e., augmenting conventional treatment in fighting cancer), relieving both cancer symptoms and treatment side-effects, and repairing or boosting up, which includes detoxifying the body, boosting immunity and energy, and enhancing quality of life [22].

Other surveys of cancer patients have highlighted the goal of health restoration and promotion. The most common reasons for using CAM cited by breast cancer patients in Ontario were to boost the immune system (63%), increase quality of life (53%), and prevent cancer recurrence (43.5%) [4]. Large numbers of both women (73%) and men (56%) in the SEER cohort in western Washington used dietary supplements, primarily to improve general health and well being (95% of supplement users) [23]. However, relatively few cite symptom treatment as reason for using CAM: 21% mentioned treating side effects of conventional cancer treatments in the Ontario survey, and only 4% of the VA patients gave this reason. [4] A survey of cancer patients in the VA found that of the 61% who took a dietary supplement, 41% cited "energy increase" as their reason [24]. When asked about benefits, 40% said it improved overall health, 21% reported increased energy, and only 9% said dietary supplements improved symptoms. Yet, an MD Anderson survey found that having received chemotherapy doubled the likelihood of its use and was the most common characteristic of users [25]. Hedderson et al. found that cancer patients' decisions to use dietary supplements are associated with more severe treatment side effects and also a stronger desire for personal control [29].

The distinction between symptom relief and more global benefits echoes the distinction between the medical model of combating specific diseases and a more broadly

understood relationship between diet and health. The concepts occasionally overlap, as in the well-established diet-heart theory linking dietary components, especially fats, to cardiac risk. However, the parallel diet-cancer theory has far less epidemiological support, and the concept of epidemic obesity in the US has apparently been embraced slowly and fitfully despite the striking data supporting it. The associations between CAM use and the healthy lifestyle and favorable socioeconomic variables, including higher educational and income levels, suggest that the broader concept of diet as a tonic, not a medicine, prevails in populations removed from severe economic adversity. As a result, the effects patients expect and perceive from Sen-Sei-Ro may have little to do with medical specifics such as the particular cancer diagnosis, the intensity of treatment and how recently it was given.

This distinction is useful for evaluating a substance taken both to obtain a global benefit, as well as to counter an array of specific symptoms. For example, antiemetic treatment against chemotherapy-induced nausea and vomiting produces quality of life benefits by reducing a specific noxious symptom complex that are much greater than the more global impact of erythropoietin on patients receiving chemotherapy. The two constructs we found correspond to patient goals for CAM identified in other studies. In another breast cancer patient cohort, CAM use was a marker of psychosocial distress, which may in part have motivated its use [33], since CAM is used more often by more seriously ill patients.

These results imply that patient-based measures of the effects CAM products must be strongly informed by patients' explanatory models of cancer "pharmacology," which may differ from their physicians', and measure the outcomes they value, according to their perspectives. Measures should focus on tonic effects on body strength and overall function as well as on symptom alleviation. If dietary supplements are not taken primarily for symptom relief, patients may not experience and report it, even if that is the reason their doctors prescribed the supplement. The stronger body patients hoped for may resist symptoms better, but the patient may consider that a lucky byproduct, not the main objective.

If the benefits of Sen-Sei-Ro and related products are likely to be global, rather than symptom-specific, investigations should target broad measures of well-being and systemic symptoms of anxiety or sadness, depression, appetite, maintaining body weight, daily activities, and socializing with others, in additional specific symptoms such as hair loss, nausea and pain. Our use of a 3-item Likert response set may be improved by using a 5-item scale, which would produce less granular data with better better statistical properties for psychometric analyses. We look forward to further development of this instrument to assess the use of this and other CAM substances in cancer patients. We plan to use these results to inform a series of focus groups to refine and supplement these items, pilot test additional items, subject the revised instrument to further validation studies and to use the final validated instrument in randomized trials of the efficacy of Sen-Sei-Ro and other CAM substances with putative health properties in cancer patients, if adequate research funding is available.

Conclusion

Respondents to our survey of Sen-Sei-Ro consumers with cancer reported favorable perceived effects from its use. Our instrument, when further validated, may be a useful outcome in trials assessing this and other CAM substances in cancer patients.

Competing interests

Drs. Talcott and Clark have consulted for and received research support from Sundory Corporation, which markets Sen-Sei-Ro. Dr. Lee is a Professor at the Kanazawa University Venture Research Laboratory (VBL), to which Sundory and Kyowa-S.S.I., Tokyo, Japan, which manufactures Sen-Sei-Ro, contribute research funding.

Authors' contributions

JAT was involved in the design of the study, the drafting of the survey, the interpretation of the results and drafted the manuscript. JAC was involved in the design of the study, the primary drafting of the survey, the execution and primary interpretation of the psychometric analyses and co-drafted the manuscript. IPL was involved in the concept and design of the study, coordinated the translation of the survey and the performance of the survey, and contributed to the draft and revisions of the manuscript. All authors read and approved the final manuscript.

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Case Reports

An Alternative Medicine, *Agaricus blazei*, May Have Induced Severe Hepatic Dysfunction in Cancer Patients

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We report three cases of patients with advanced cancer who showed severe hepatic damage, and two of whom died of fulminant hepatitis. All the patients were taking *Agaricus blazei* (Himematsutake) extract, one of the most popular complementary and alternative medicines among Japanese cancer patients. In one patient, liver functions recovered gradually after she stopped taking the *Agaricus blazei*, but she restarted taking it, which resulted in deterioration of the liver function again. The other patients who were admitted for severe liver damage had started taking the *Agaricus blazei* several days before admission. Although several other factors cannot be completely ruled out as the causes of liver damage, a strong causal relationship between the *Agaricus blazei* extract and liver damage was suggested and, at least, taking the *Agaricus blazei* extract made the clinical decision-making process much more complicated. Doctors who are aware of their patients taking the extract may accept it probably because they believe there is no harm in a complementary and alternative medicine. When unexpected liver damage is documented, however, doctors should consider the use of the *Agaricus blazei* extract as one of its causal factors. It is necessary to evaluate many modes of complementary and alternative medicines, including the *Agaricus blazei* extract, in rigorous, scientifically designed and peer-reviewed clinical trials.

Key words: alternative medicine – Agaricus blazei – fulminant hepatitis

INTRODUCTION

Complementary and alternative medicine (CAM) is defined as a medical intervention which is not taught widely at medical schools or is not generally available in hospitals (1). The use of CAM has become common among many cancer patients worldwide. A summary of 26 surveys conducted across 13 counties estimated the prevalence of the use of CAM at 31.4% of all cancer patients, ranging from 7 to 64% (2), and this market may be growing as fast as 30% annually in the USA (3).

Despite the modest gains achieved in cancer treatment with multimodality therapies in the last decade, the majority of cancer patients with advanced-stage die of refractory and disseminated disease. Therefore, cancer patients who do not improve or feel beneficial effects from ordinary medicine expect CAM to cure their disease, prolong life, alleviate symptoms, improve their quality of life and boost their immune system. They value CAM for its medicinal potential. Another reason for using CAM is that they are believed not to have severe toxicities and may have the potential to control adverse effects caused by chemotherapy.

The great majority of patients taking CAM probably do so in conjunction with standard cancer therapies and usually do not stop using ordinary medicine that physicians recommend. A concern is that these adjunctive practices might pose risks to patients. There are theoretical reasons for thinking that some vitamin or herbal medicine might biochemically interfere with chemotherapy or radiation treatments, adversely alter treatment compliance, or cause side effects such as hepatic injury (4–6).

Agaricus blazei (Himematsutake) is a mushroom-derived compound and is widely used among cancer patients in

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Japan. As is the case with other CAM compounds, no scientific evidence supports their safety or efficacy. We report here three cancer patients who took *Agaricus blazei* extract and showed severe hepatic dysfunction.

CASE REPORT

CASE 1

A 66-year-old woman with stage IIIC ovarian cancer was scheduled to receive post-operative combination chemotherapy with cisplatin and cyclophosphamide (CDDP + CPA) for six cycles. She had no particular past history including allergic reaction. Following the first cycle of chemotherapy, she had a fever of 39.6°C and elevation of transaminases (peak AST:392, ALT:292, T-bil:4.7) was documented (Fig. 1). Liver function was recovered thereafter. The second cycle of the chemotherapy was given on the due date and the same events occurred. She was diagnosed as having chemotherapy-induced hepatitis and the following doses and all other medications were withheld. However, the transaminase levels continued to fluctuate significantly for unknown reasons. Her disease recurred 8 months after the operation but continuing elevated transaminase prevented the sufficient use of systemic chemotherapy. She disclosed to her doctor at her terminal stage that she had been taking *Agaricus blazei* extract at the time of chemotherapy following her friend's recommendation. She was advised to withhold its use and her liver function returned to normal.

CASE 2

A 58-year-old woman was admitted to our hospital because of general fatigue. She had had a right mastectomy for her stage IIIA breast cancer 9 months previously and had received six cycles of cyclophosphamide + doxorubicin + 5FU (CPA + ADR + 5FU:CAF regimen) for adjuvant chemotherapy. The interval duration from the cessation of chemotherapy to this admission was 3 months.

Upon admission, AST, ALT, *t*-bilirubin and prothrombin time were 231 IU/l, 1226 IU/l, 6.6 mg/dl and 18 s respectively, and no causative factors such as drugs, viruses or alcohol intake were documented. Recurrence of breast cancer was not demonstrated. She had started to take *Agaricus blazei* extract a few days before her admission. The liver damage and her level of consciousness gradually deteriorated on the day following admission. She subsequently died with severe liver damage 7 days after her admission.

CASE 3

A 48-year-old woman with metastatic breast cancer in the bone started to receive chemotherapy with doxorubicin and cyclophosphamide (ADR + CPA). Before the chemotherapy, serological tests revealed that she was a chronic carrier of hepatitis B virus (HBV) (positive for HBs antigen and anti-HBe antibody and negative for HBe antigen) and the serum transaminase levels were normal. After three cycles of the chemotherapy, she complained of appetite loss (National Cancer Institute Common Toxicity Criteria (NCI CTC) version 2, grade 2), nausea and vomiting (NCI CTC version 2, grade 2). She was admitted to the hospital because of hepatic dysfunction (AST, 5265; ALT, 7365; T-bil, 5.3). A test for HBV-DNA with a polymerase chain reaction assay indicated viral replication. She said she had taken *Agaricus blazei* extract and no other drugs for several days before admission. She was diagnosed as having acute hepatitis and it developed rapidly. She was transferred to another hospital for plasma exchange therapy but died of fulminant hepatitis 6 days after.

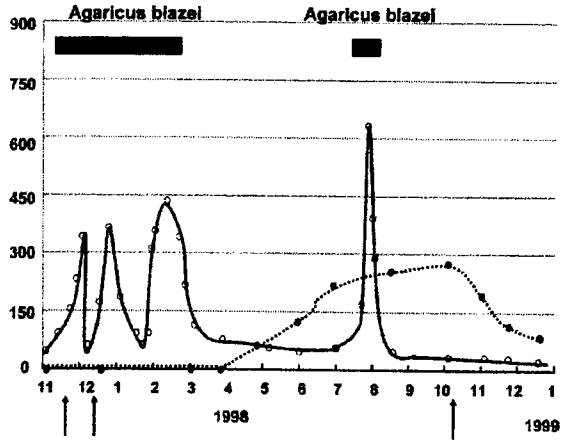

Figure 1. Clinical course of Case 1 with AST and CA125. Continuous line, AST; dashed line, CA125; vertical arrow, administration time of the each cycle of the chemotherapy; solid square, period of taking the *Agaricus blazei* extract.

DISCUSSION

We report three cases that showed severe hepatic dysfunction during the course of cancer treatment or follow-up, two of whom died of fulminant hepatitis. All of them had episodes of oral intake of *Agaricus blazei* extract, but no other conventional or CAM regimens were used. It is indeed difficult to clearly identify the *Agaricus blazei* extract as the cause of the liver dysfunction, because other causative factors such as cancer chemotherapy and hepatitis virus cannot be completely ruled out. However, it should be noted that concurrent use of the *Agaricus blazei* extract made the differential diagnosis process rather complicated.

In case 1, the liver function recovered gradually after the patient stopped taking the *Agaricus blazei* extract, but when she restarted taking the extract, it deteriorated again. This time course suggests a strong causal relationship between the *Agaricus blazei* extract and the liver dysfunction.

The patient in case 2 told her doctor at the time of admission that she had started taking the *Agaricus blazei* extract

several days before admission. No other causative factors were documented. This episode strongly suggests that the *Agaricus blazei* extract induced the fatal liver dysfunction.

The third patient was a chronic carrier of HBV. It has been well documented that cancer chemotherapy such as CHOP (cyclophosphamide + doxorubicin + vincristine + prednisolone) activates hepatitis B virus replication in patients in the chronic carrier status (7,8), especially as a result of high doses of steroid. However, reactivation of hepatitis by AC regimen at the standard dose has not yet been reported. Although the ultimate reason of the severe hepatic damage could not be known, it cannot be ruled out that the use of the *Agaricus blazei* extract might have some adverse influence on the nonreplicable phase of HBV infection.

Some CAM agents have been reported to be toxic and may interact with other medications (9,10). It has also been reported that some herbs photosensitize the skin and cause severe reactions when used in combination with radiation therapy (9).

In general, patients are reluctant to report their use of CAM to their doctors (11). A recent study suggests that physicians are unaware of 80–90% of all CAM use if the patients do not directly inform the physician about such practices (12). Physicians should take the initiative and have discussions about the usage of CAM with their patients. A close doctor–patient relationship including good communication is one way to limit the use of ineffective or toxic CAM agents, saving the patients from abandonment or disinformation. Especially when unexpected liver damage is documented, doctors should consider the use of the *Agaricus blazei* extract as one of the causal factors for the phenomenon.

In the available studies concerning practitioners of CAM, it was found that 60% of the providers of such treatments were medical physicians. The remaining 40% were chiropractors, naturopaths, homeopaths, or nutritionists, some of whom were trained in institutions with marginal academic standards (13). Physicians who provide CAM should acknowledge that many CAM lack sufficient safety and efficacy data.

CAM today represents a medical and social phenomenon that cannot be ignored and requires the need for proper research. The broad dissemination of untested therapies is an unacceptable practice. CAM, including the *Agaricus blazei* extract should be evaluated in rigorous, scientifically designed clinical trials (14).

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Preliminary report

Effects on gene expression and viral load of a medicinal extract from *Agaricus blazei* in patients with chronic hepatitis C infection

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Abstract

Extracts from the mushroom *Agaricus blazei* Murill (AbM) are used extensively as a non-prescription remedy against cancer and infections, including hepatitis. We previously demonstrated a potent immunomodulating effect of a particular preparation on monocytes in vitro, and a protective effect on bacterial infections in mice. Here we report the effect on gene expression in peripheral blood cells from four chronic hepatitis C patients, using global (29 k) oligo-based, single channel microarrays. The viral load was slightly, but not significantly, decreased after 1 week of AbM treatment. The cytokine genes most strongly induced in vitro were not induced in vivo. The more notable changes in mRNA levels were related to genes involved in the G-protein coupled receptor signalling pathway, in cell cycling, and in transcriptional regulation. The results suggest that the β-glucans of the extract, which presumably are responsible for cytokine induction, did not readily enter the blood, while other components, such as substances proposed to have anticancer effects, were active in the blood.

Keywords: *Agaricus blazei* Murill; Microarray; Gene expression; Hepatitis C virus; Cancer; G-protein coupled receptors

1. Introduction

Agaricus blazei Murill (AbM) is widely used for non-prescript, medicinal purposes, both as an edible mushroom and in the form of extracts. According to tradition, it helps against a variety of diseases, including cancer, diabetes, arteriosclerosis and hepatitis. In recent years, considerable research has been carried out to investigate the putative effects. Several reports indicate positive results in the treatment of cancer [1–4], and the immunomodulating potential of extracts seems to be well documented from in vitro studies, as well as experiments with mice [5–10]. One report found an inhibition of equine encephalitis virus in cell culture [11]. We have recently shown that the AbM preparation used in the present experiments has potent immunomodulating effects on human monocytes in vitro [12], and protects against *Streptococcus pneumonia* infection [13] and lethal septicaemia [14] in mice. The information listed above led to an acceptance from the ethical committee to examine the effect on chronic, non-treatable hepatitis C virus (HCV) infections in humans.

Abbreviations: AbM, *Agaricus blazei* Murill; HCV, hepatitis C virus; GO, gene ontology; HUGO, human genome organisation; MIAME, minimum information about a microarray experiment.

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AbM extracts are rich in β-glucans, which presumably stimulate the immune system by binding to Toll-like receptor 2 (TLR2) and dectin-1 (CLECSF12) [15,16]. The binding activates MYC88 [15] and causes the induction of various cytokines [12]. It is not obvious, however, to what extent the β-glucans are absorbed by the human digestive system. One purpose of the present study was to indicate whether the immunomodulating β-glucans are transferred to the blood by examining the induction of signature cytokines in blood cells.

Smaller and more soluble ingredients, such as ergosterol, pyroglutamate and fragments of β-glucans, have been postulated to be responsible for the antitumor activity [17–19]. Again, by examining blood cells, it might be possible to find changes in gene expression indicative of the cytostatic or apoptotic effects observed in these papers. Thus, besides investigating a possible beneficial effect on patients with chronic HCV infection, the present effort was directed at elucidating changes in the gene expression of blood cells.

2. Materials and methods

Five patients (four males, one female, age 46–58 years) were recruited from the Ullevål University Hospital. They had at least 1 year of HCV infection, did not respond to interferon treatment, and underwent no specific anti-viral therapy (interferon and/or ribavirin), or other specific medication, during the last 5 months prior to the current experiment. The experimental treatment with AbM extract (Gold label from ACE Co., Ltd., Gifu-ken, Japan) was approved by the Norwegian Medicinal ethical committee, and all patients signed a consent form.

HCV in plasma was quantified using the Quantiplex™ bDNA HCV RNA Assay version 2 (Chiron, Emeryville, CA). The patients had from 1.5 to 12 million copies/ml. They were given the AbM treatment regime recommended by the manufacturer, i.e., 20 ml three times a day for 1 week (Table 1). Blood samples were taken prior to start, after 4 days and after 7 days, using one EDTA vacutainer for plasma and one PAXgene tube (PAXgene™ Blood RNA System, Qiagen). The PAXgene tubes, which are specifically designed to preserve RNA from blood for microarray experiments [20], were frozen and kept at −20 °C until extraction according to manufacturer's recommendations. The extraction included DNase treatment, and gave from 3–7 μg of RNA. RNA concentration and quality were determined using UV spectrophotometry (NanoDrop Technologies, Wilmington, DE), as well as microcapillary electrophoresis on a Bioanalyzer 2100 (Agilent Technologies, Palo Alto, CA). RNA from one patient was not of sufficient quality for microarray experiments. Samples from before and after 7 days of treatment from the other 4 patients were analysed as to gene expression using the Human Genome Survey Microarrays V2.0 and the Applied Biosystems Expression Array System labelling (Applied Biosystems, Foster City, CA). The arrays included oligos designed to detect the full complement (29 098) of human genes. Labelled RNA and arrays were hybridized (55 °C, 16 h) on a Stuart Orbital Incubator SI50

Table 1
Select genes with changed expression following AbM treatment

Gene symbol (HUGO)	Gene name – description	Fold change	*p*-value
Up-regulated			
CDC2L5	Cell division cycle 2-like 5 – cyclin-dependent protein kinase, master switches in cell cycle control, apoptosis	1.7	0.015
CLECSF14	C-type lectin domain family – cell–cell signalling and roles in inflammation and immune response	1.3	0.043
CRADD	CASP2 and RIPK1 domain containing adaptor – a death-domain-containing protein, induce apoptosis	1.6	0.03
DNASE1L3	Deoxyribonuclease 1-like 3 – mediates the breakdown of DNA during apoptosis	5.2	0.009
HOXA1	Homeobox A1 – a DNA-binding transcription factor belonging to the homeobox genes	2.6	0.048
IFNAR1	Interferon receptor 1 – receptor for interferons alpha and beta, function as an antiviral factor	5.3	0.021
MEF2C	MADS box transcription enhancer factor 2 – a transcription enhancer factor also referred to as myocyte enhancer factor 2C	1.4	0.033
NFATC3	Nuclear factor of activated T-cells – plays a role in the regulation of gene expression in T cells and immature thymocytes	1.3	0.018
PHTF2	Putative homeodomain transcription factor 2	1.5	0.001
PTGIR	Prostaglandin I2 receptor – member of G-protein coupled receptor family 1	3.0	0.027
RARB	Retinoic acid receptor, beta – a member of the thyroid-steroid hormone receptor superfamily of nuclear transcriptional regulators. Thought to limit the growth of many cell types by regulating gene expression	1.3	0.024
TADA2L	Transcriptional adaptor 2 – a transcriptional activator adaptor	1.7	0.01
TAF1	RNA polymerase II, TATA box binding protein associated factor – helps coordinate transcriptional activation	6.8	0.004
UBTF	Upstream binding transcription factor, RNA polymerase I	4.5	0.016
Down-regulated			
PDGFRA	Platelet-derived growth factor receptor – a cell surface tyrosine kinase receptor for PDGF mitogens	0	0.041
ORC2L	Origin recognition complex, subunit 2-like – part of complex essential for initiation of DNA replication	0.7	0.036

Fold changes reflect average values in the four patients, a 0 implies that the gene was not at all expressed in the post-treatment samples. The *p*-values were calculated by the Feature Subset Selection function in J-Express.

(Barloworld Scientific, Italy), washed on a Heidolph Duomax 1030 (Rose Scientific, Edmonton, Canada), and subsequently scanned on a 1700 Chemiluminescent Microarray Analyzer (Applied Biosystems).

The Quality Check Report for the microarrays gave normal values. J-Express [21] was used to filter the data, i.e., controls, flagged spots and spots with signal to noise < 3 were removed. The intensities of the different arrays were normalized using the Quantile Normalize All Arrays function. The arrays were grouped as to before or after treatment, and the Feature Subset Selection function (an adopted *T*-test) was used to find genes significantly ($p<0.05$) up- or down-regulated as a consequence of treatment. The lists were transferred to Excel and subsequently uploaded to GeneTools (http://www.genetools.microarray.ntnu.no/adb/) for gene ontology (GO) analyses. In GeneTools the up- and down-regulated genes were compared as to Biological Processes and Molecular Function with the Target–Target test, and both lists were compared to the complete list of expressed genes using the Target–Master test (based on gene annotations available as of December 2005). The following internet-based resources were employed to obtain further information as to gene function: PubGene (http://www.pubgene.org/), Panther (https://panther.appliedbiosystems.com/), and GeneCards (http://www.genecards.org/index.shtml). HUGO gene symbols are preferentially used. The microarray data are submitted to the Gene Expression Omnibus (http://www.ncbi.nlm.nih.gov/geo/) with the accession no GSE3983.

3. Results and discussion

The present clinical evaluation was prompted by recent positive results for a particular AbM extract in mice and in cell culture studies [12–14]. One aim was to investigate a possible role for the extract in the treatment of HCV patients who failed to respond to regular treatment. Although the average ($n=5$) titre of virus was slightly lower after one week on AbM (5.3 compared to 5.8 million copies of virus per ml plasma), the difference was clearly not significant.

The main purpose, however, was to examine the systemic effect of AbM when administered orally. Presumably changes in gene expression of peripheral blood cells would reflect the impact of substances taken up in the blood. Microarray gene expression experiments were therefore carried out on samples from 4 patients taken before and after treatment (RNA from the last patient was not of sufficient quality). The subsequent analyses concluded that some 14976 genes were expressed in at least one of the 8 samples, corresponding to 13,931 annotated genes. Using the Feature Subset Selection function in J-Express, a list of 220 genes (204 annotated) were found to be significantly up-regulated ($p<0.05$) when comparing after treatment samples with before treatment; and, correspondingly, 65 genes (58 annotated) were down-regulated. The observation that more genes were up-regulated compared to down-regulated is in line with the previous in vitro study [12], and is, furthermore, expected as medicinal substances are more likely to activate rather than turn off genes.

The assumed β-glucan receptors, TLR2 and CLECSF12 [16,22], as well as the main down-stream signalling protein MYD88 [15] were expressed in all samples, but not appreciably changed; with the possible exception of the TLR2 receptor, which had increased expression in three patients (the average increase of 1.3 was not statistically significant). Moreover, the cytokines and other immune related genes that were highly induced in vitro, such as IL8, IL1B, SCYA4, CCL3, CXCL3 and PTGS2, were not induced in vivo. The diversity of cells present in the blood may mask changes in expression appearing only in certain subsets of cells, but if the induction of for instance IL8 and IL1B had been in the order of magnitude seen in monocytes in culture, the change should be easily discernable in vivo as well. Thus, the results suggest that the β-glucan part of the extract was not transported into the blood in appreciable quantities.

Some immunorelated genes were induced in vivo. For example, the interferon receptor 1 (IFNAR1) was up 5.3 times; and CLECSF14, a member of the C-type lectin domain family involved in inflammation and immune response, was also slightly up-regulated. In the GO analyses, the biological process with the most significantly changed expression profile was the G-protein coupled receptor protein signalling pathway (GO:0007186). Genes involved in this process were overrepresented both in the list of 204 up-regulated genes (10/343, $p=0.028$) and in the list of 58 down-regulated genes (5/343, $p=0.007$). There are many G-protein coupled receptors serving different functions, including the chemokine receptors. The results suggested that AbM causes a change in the use of these signalling pathways.

Another interesting observation was that a large number of the genes on the two lists are involved in cell cycling. By considering the function of each of these genes, it became apparent that those on the up-regulated list would be expected to work in the direction of either inhibiting cell division or inducing apoptosis (e.g., CDC2L5, CRADD, DNASE1L3 and RARB); while those on the down-regulated list would be expected to stimulate growth (e.g., PDGFRA and ORC2L). It is tempting to associate this finding with the published positive effects of AbM extracts on cancer [1–4], possibly related to low molecular weight substances present in the extract [17–19].

Several genes on the up-regulated list are involved in transcriptional regulation (e.g., HOXA1, NFATC3, PHTF2, TADA2L, TAF1 and UBTF). Presumably this observation reflects a change in functional status of peripheral blood cells.

The immunomodulating effect of AbM observed in the monocyte cell culture study did not manifest itself in vivo, possibly because the β-glucans presumed to be the main agent responsible for this effect were not readily absorbed from the intestines. It should also be noted that most of the work concerning immunomodulating and anti-infection effects were either done in vitro or in mice [6–9,11,13,14,23]. In the present study we used the dosage suggested by the manufacturer, the quantity typically used on mice may be relatively larger, or the uptake of β-glucans more efficient. The present results do not warrant recommendation of AbM for the treatment of HCV infections. The induction of the interferon receptor (IFNAR1) is,

however, intriguing. An increase in this receptor may be useful for patients who do not respond to interferon treatment.

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ORIGINAL ARTICLE

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Use of complementary and alternative medicine by patients with urologic cancer: a prospective study at a single Japanese institution

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Abstract *Objectives:* We prospectively evaluated the prevalence and predictors of complementary medicine (CAM) use among Japanese patients with urologic cancer 1 year after diagnosis. *Patients and methods:* A total of 349 patients with newly diagnosed urologic cancer answered a self-administered questionnaire on CAM use 1 year after diagnosis. General-health-related quality of life (GHQL) of the patients was also assessed at diagnosis and 1 year after diagnosis using the Medical Outcome Study Short Form-36 (SF-36). The overall prevalence, types of CAM used, and costs of CAM were assessed. The effects of several variables including GHQL at baseline and 1 year after treatment on the prevalence of use of CAM were evaluated. *Results:* A total of 164 respondents (47%) admitted using some type of CAM, of which 73 (45%) had used multiple types. "Health food," in particular extract from *Agaricus blazei*, was the most common type of CAM used. CAM users had significantly lower scores for social function, general health perception, and vitality domains than CAM non-users 1 year after diagnosis. This tendency was more marked in users of multiple types of CAM. *Conclusions:* "Health food," including extract from *A. blazei*, was the most commonly used CAM in Japan. The prevalence of CAM use did not differ between patients with prostate cancer and those with urologic cancer other than prostrate cancer. CAM users, especially those who used multiple types of CAM, had lower GHQL scores than non-users of CAM.

Keywords Urologic cancer · Alternative medicine · Health survey · General-health-related quality of life · Epidemiology

Introduction

In the United States, "alternative" or "complementary medicine" (CAM) is defined as the set of treatments whose efficacy has not been proven by the National Institutes of Health Office of Alternative Medicine. This type of medicine has gradually gained attention worldwide since the study by Eisenberg et al. [1]. Recently, many studies have been conducted to elucidate the prevalence of use of CAM by patients with urologic disease in several western countries [2–10]. However, all such studies included only patients with prostate cancer, and no study determined the prevalence of CAM use in patients with types of urologic cancer other than prostate cancer. Furthermore, most of such studies were performed in cross-sectional fashion.

In this prospective study, we attempted to determine the prevalence of CAM use in patients with urologic cancer, including renal cancer, renal pelvic cancer, ureteral cancer, bladder cancer, prostate cancer, and testicular cancer, 1

year after diagnosis. We also attempted to elucidate the factors affecting CAM use.

Patients and methods

From October 2000 to December 2003, a total of 511 patients who were newly diagnosed with urologic cancer underwent treatment at Kurashiki Central Hospital. In this group, patients with highly advanced cancer and those unaware of being diagnosed with cancer were excluded, leaving 450 patients as candidates for inclusion in this study. We explained the main purpose of this study to these patients and obtained their informed consent. No financial reimbursement was given to the patients for filling out the questionnaire.

For assessment of general-health-related quality of life (GHQL), the Medical Outcome Study Short Form-36 (SF-36) [11] Japanese version 2.0 was used. This questionnaire consists of 36 self-administered questions that quantify GHQL using eight multi-item scales, physical function (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health perception (GH), vitality (VT), social function (SF), role limitations due to emotional problems (RE), and mental health (MH). The eight scales were scored separately from 0 to 100, and their scores were used for comparison between the two groups. The scores were adjusted for comparison with the general population, with a score of 50 representing normal function and a standard deviation of 10 points. In this questionnaire, a higher score represents a better quality of life. It was translated into Japanese and its validity and reliability were tested by Fukuhara and Koshinski [12] in a Japanese population chosen randomly from different generations. This questionnaire was administered to the patients just after cancer diagnosis and 1 year after diagnosis. A seven-item self-administered questionnaire on CAM, which was used in our previous study [13], was also distributed to patients 1 year after diagnosis. The types of CAM followed the items used in our previous study [13], except for the addition of the item on "health foods." Other medical information was extracted from charts.

The effects of age at diagnosis (69 years or younger versus 70 years or older), gender, calendar year at diagnosis, type of disease (prostate cancer versus others), disease stage (localized versus metastasized), disease status 1 year after diagnosis (no evidence of disease plus stable disease versus progressive disease), marital status, family structure, patients' income, and patients' final educational status, and eight domains of the SF-36 at baseline and 1 year after diagnosis on the prevalence of use of CAM, use of at least one type of CAM and use of multiple types of CAM, were analyzed.

Student's t test or chi-square test was used for statistical analysis. P values of less than 0.05 were considered significant.

Results

Demographic characteristics

Of the 450 eligible patients, 349 (78%) answered the questionnaire. The patients' characteristics are shown in Table 1. Almost half of the patients had prostate cancer alone. Small proportions of the patients had metastatic disease or were not living with spouse. Sixty percent of patients had retired or had no current occupation. Among the eight domains of the SF-36, PF at 1-y after diagnosis was significantly lower than that at baseline (44.8 versus 46.8, p=0.029), and MH at 1-y after diagnosis was significantly higher than that at baseline (51.7 versus 49.1, p=0.001).

Overall prevalence of CAM use

A total of 164 (47%) of the 349 patients had used some type of CAM. Thirty-three of these 164 patients (20%) had already begun to use CAM before cancer diagnosis. Twenty-one (13%) and 26 patients (16%) began CAM use within 3 months after initiation of our treatment and 3 months

Table 1 Patients characteristics

Age		Median 69 (range 21–92)
	<70:≥70 years	195:154
Gender	Male:Female	302:47
Type of disease	Prostate cancer alone	171
	Bladder cancer alone	84
	Renal cancer alone	55
	Upper urinary tract cancer alone	23
	Testicular cancer alone	6
	Double urologic cancer	9
Metastasis	Yes:No	24:325
Disease status 1-y after diagnosis	No or stable:progressive	279:70
Spouse living together	Yes:No	311:38
Other family living together	Yes:No	176:173
Income (year)	No or retired	211
	<5,000,000	49
	5,000,000≤10,000,000	34
	≥10,000,000	13
	No answer	42
Final education	No university training	252
	University training	57
	No answer	50
Calendar year at diagnosis	2000–2001	123
	2002	110
	2003	116

Table 2 Types of CAM used

Types of CAM	Total no. of CAM used	Percent among all CAM used (%)	No. of patients using CAM	Percent among CAM users (%)
Healthy food	187	64	119	73
Extract from *Agaricus blazei*	52	18	52	32
Propolis	21	7	21	13
Extract from *Curcuma longa*	16	5	16	10
Others	103	35	61	37
Vitamins	35	12	35	21
Oriental herbal medicine	16	5	16	10
Massage	13	4	13	8
Prayer or religious practice	7	2	7	4
Dietary adjustments or fasting	5	2	5	3
Chiropractic therapy	4	1	4	2
Magnets	4	1	4	2
Others	22	8	21	13
Total number	293	100	164	100

after initiation of our treatment or later, respectively. Fifty-one patients (31%) did not indicate the time of initiation of CAM use.

Types of CAM used and Costs of CAM

Of the 164 patients who had tried CAM, 73 (45%) had used multiple types of CAM. Table 2 presents a summary of types of therapies used and costs per month. The most commonly used therapy was "health food", which 119 patients (73%) had tried. Following "health food," vitamins were the second most popular type of CAM, used by 35 patients (21%). Extract from *Agaricus blazei*, a type of mushroom, was the most commonly used "health food" by 52 patients (32%). Propolis and extract from *Curcuma longa* followed, used by 21 (13%) and 16 (10%) patients, respectively. Fifty-nine percent of patients had spent ¥1,000–50,000/month for CAM.

Predictors of CAM use

Most variables tested—including age at diagnosis, gender, calendar year at diagnosis, type of disease, disease stage, disease status 1 year after diagnosis, marital status, family structure, patients' income, and patients' final educational status—had no impact on the prevalence of CAM use (Table 3). On the other hand, users of CAM had significantly lower SF, GH, and VT scores than non-users 1 year after diagnosis (Fig. 1). When we compared the 73 patients who used multiple types of CAM with the other patients who used no or only a single type of CAM for scores on the SF-36, SF, RE, and MH at baseline and RP, SF, VT, BP, and RE 1 year after diagnosis were significantly lower in the former patient group than in the latter (Fig. 2).

Discussion

Several studies on the prevalence of CAM use by patients with prostate cancer have recently been reported [2–10, 13]. Generally, 18–43% of the patients were reported to use some type of CAM at the time these studies were being performed. In the present study, 47% of patients with prostate cancer admitted using some type of CAM. The type of CAM most often used was "health food," including extracts from *A. blazei* and *C. longa*, and Propolis. This tendency of prevalent consumption of "health food" as a type of CAM is characteristic of Japanese patients, since recent studies using large patient populations from the United States, Canada, and Austria reported that the most

Table 3 Prevalence of CAM users

	Categories	CAM users	Users of Multiple CAM
Age	<70:≥70 years	91 (47%):73 (47%)	46 (24%):27 (18%)
Gender	Female:Male	26 (55%):138 (46%)	12 (26%):61 (20%)
Type of disease	Prostate cancer:Others	81 (47%):83 (47%)	34 (20%):39 (22%)
Metastasis	Yes:No	13 (54%):151 (46%)	9 (38%):64 (20%)
Disease status 1-y after diagnosis	No or stable:Progressive	131 (47%):33 (47%)	60 (22%):13 (19%)
Spouse living together	Yes:No	146 (47%):18 (47%)	66 (21%):7 (18%)
Other family living together	Yes:No	79 (45%):85 (49%)	40 (23%):33 (19%)
Occupation	No or retired:Incumbent:No answer	89 (42%):50 (52%):25 (60%)	38 (18%):23 (24%):12 (29%)
Final education	Below university:University:No answer	112 (44%):30 (53%):32 (64%)	45 (18%):14 (25%):13 (26%)
Calender year at diagnosis	2000–2001:2002:2003	61 (50%):50 (45%):53 (46%)	24 (20%):28 (25%):21 (18%)

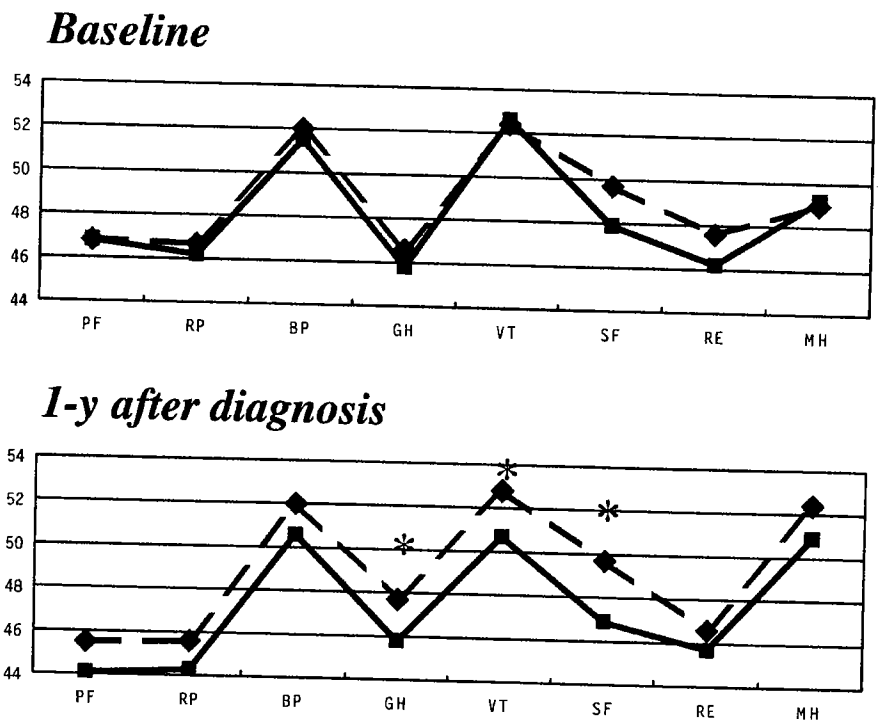

Fig. 1 SF-36 at baseline and 1-y after diagnosis. CAM users (*solid line*) versus nonusers (*dashed line*). *$p<0.05$

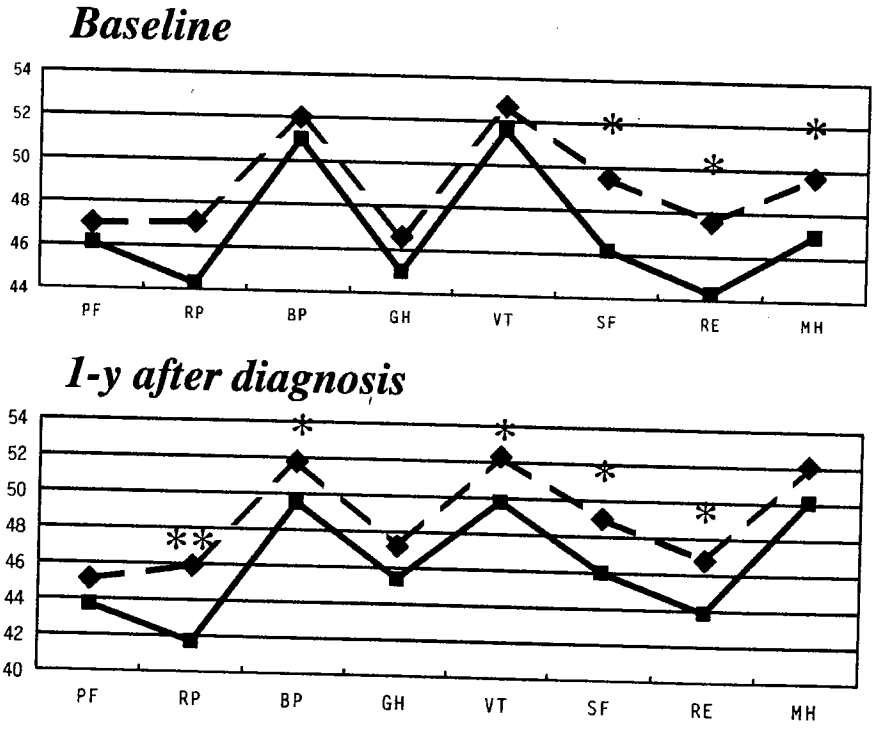

Fig. 2 SF-36 at baseline and 1-y after diagnosis. Users of multiple types of CAM (*solid line*) versus nonusers plus users of a single type of CAM

commonly used types of CAM were saw palmetto, selenium, and vitamins, especially vitamin E [5, 6, 8]. Also, in our previous study, extracts from *A. blazei* and *C. longa*, and Propolis were the types of CAM most commonly used, and were classified as "herbal medicines" [13]. Popular types of CAM appear to differ from country to country, as Chinese, Hawaiian, and Korean studies have shown [14–16].

The present study revealed another important finding: that the prevalence of CAM use was the same for patients with prostate cancer as for those with urologic cancer other than prostate cancer. Previous studies considered only patients with prostate cancer, and no data were available on the prevalence of CAM use in patients with other urologic cancers, including renal, bladder, and testicular cancers. Our patients with non-prostate urologic cancers most commonly used "health food," like those with prostate cancer (data not shown). Since saw palmetto, one of the most commonly used types of CAM in western countries, is considered prostate-specific, it is unknown whether the prevalence of CAM use in patients with other urologic cancer is similar to that in patients with prostate cancer in these countries.

Most of the variables tested in the present study had no impact on prevalence of CAM use. Among these variables, gender, disease stage, patients' income, and final educational status have been frequently reported as predictors of CAM use [1, 5, 7, 8, 17–21]. Although our study did not determine the predictive values for these variables, our observation was not conclusive. Since only small portions of our patients were female, had metastatic disease, or had a current occupation, there was considerable bias in the analysis of predictors of CAM use. Patients with metastatic disease used multiple types of CAM marginally more frequently than those without it (p=0.07). The Japanese school system changed fundamentally in 1947, and the educational system before this revision cannot be simply compared with the new system, which follows the western educational system. This makes analysis of the relationship between prevalence of CAM use and final educational status very difficult.

Various aspects of general-health-related quality of life (GHQL), which were assessed using the SF-36, were significantly related with CAM use. Lower GHQL, especially at 1-y after diagnosis, was a positive predictor of CAM use. This finding is compatible with those of most previous studies of patients with breast cancer [21–23], prostate cancer [8, 13], or other types of cancers [20, 24]. This tendency of lower GHQL became even markedly stronger for patients who desired to use multiple types of CAM. Burnstein et al. [22] reported that choice of CAM could be viewed as a 'marker for distress', and Moschen et al. [21] reported that a subgroup of patients using many types of CAM appeared to have considerable adjustment problems. On the other hand, Davidson et al. [25] reported that cancer patients who opted for CAM had higher levels of fighting spirit and anxious preoccupation. Overall, our observations and those of others suggest that use of CAM strongly depends on the psychological characteristics of individual patients, regardless of other contexts including disease stage and status. The psychological stresses on cancer patients who opt to use CAM need to be evaluated.

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Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, *Agaricus blazei Murill* Kyowa, in gynecological cancer patients undergoing chemotherapy

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Abstract. Ahn W-S, Kim D-J, Chae G-T, Lee J-M, Bae S-M, Sin J-I, Kim Y-W, Namkoong S-E, Lee IP. Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, *Agaricus blazei Murill* Kyowa, in gynecological cancer patients undergoing chemotherapy. *Int J Gynecol Cancer* 2004;**14**:589–594

A mushroom extract, *Agaricus blazei Murill* Kyowa (ABMK), has been reported to possess antimutagenic and antitumor effects. Here, we investigate the beneficial effects of ABMK consumption on immunological status and qualities of life in cancer patients undergoing chemotherapy. One hundred cervical, ovarian, and endometrial cancer patients were treated either with carboplatin (300 mg/m^2) plus VP16 (etoposide, 100 mg/m^2) or with carboplatin (300 mg/m^2) plus taxol (175 mg/m^2) every 3 weeks for at least three cycles with or without oral consumption of ABMK. We observed that natural killer cell activity was significantly higher in ABMK-treated group (ANOVA, $n = 39$, $P < 0.002$) as compared with nontreated placebo group ($n = 61$). However, no significant difference in lymphokine-activated killer and monocyte activities was observed in a manner similar to the count of specific immune cell populations between ABMK-treated and nontreated groups. However, chemotherapy-associated side effects such as appetite, alopecia, emotional stability, and general weakness were all improved by ABMK treatment. Taken together, this suggests that ABMK treatment might be beneficial for gynecological cancer patients undergoing chemotherapy.

KEYWORDS: alternative therapy, *Agaricus blazei Murill* Kyowa, gynecological cancer, quality of life.

Gynecological cancer is an important cause of death in women worldwide. In particular, cervical cancer is caused mostly by infection with a high-risk group of human papillomavirus (HPV)[1–3]. In particular, two HPV oncogenic proteins, E6 and E7, play a critical role in inducing cervical cancers by interacting with p53 and pRB for the inactivation of these cellular regulatory proteins, respectively[4,5]. Multimodal chemotherapy is one of the therapeutic modalities for the patients with cervical cancer. Ovarian cancer is also a

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highly lethal disease. Owing to an asymptomatic course of early disease stage, most ovarian cancers are diagnosed at an advanced stage. This is related with poor prognosis for ovarian cancers. Despite great progress in treating gynecological cancer patients in the last three decades, recurrent or persistent cancer has been problematic. Chemotherapy has made a significant advance in the treatment of cancer patients. However, chemotherapeutic agents cause a variety of severe and life-threatening side effects, such as severe immunosuppression and bone marrow depression, adding more importance to developing any regimens for reducing side effects of the chemotherapy.

A mushroom extract, *Agaricus blazei Murill* Kyowa (ABMK), has been reported to have antimutagenic effects[6]. Furthermore, ABMK possesses tumoricidal and immunopotentiating effects[7–11]. In one study, intratumoral injection of the *A. blazei* extract resulted in the infiltration of natural killer (NK) cells in the tumor sites and increased NK cell activity in animals[7,12]. Its major component, D-glucan, has been ascribed to these antitumor properties[7,8,10,11]. At present, ABMK is consumed as a food or tea worldwide due to its expected medicinal properties.

In this study, we evaluated whether ABMK consumption might have any beneficial effects in gynecological cancer patients undergoing chemotherapy with either carboplatin (300 mg/m^2) plus VP16 (etoposide, 100 mg/m^2) or carboplatin (300 mg/m^2) plus taxol (175 mg/m^2) in our clinic in the department of obstetrics and gynecology, Kangnam St. Mary's Hospital. We observed that ABMK exerted some positive effects on innate NK cell activity and, in general, on the quality of life in patients undergoing chemotherapy. This clinical finding suggests that ABMK consumption might be beneficial for maintaining immune activities as well as the quality of life in gynecological cancer patients undergoing chemotherapy.

Materials and methods

Cohorts

One hundred gynecologic patients who visited the Department of Obstetrics and Gynecology, Kangnam St. Mary's Hospital (Seoul, South Korea) in the 3-year period from 1999 to 2001 were recruited for this investigational trial. The patients were randomized for treatments with ABMK and placebo in a blinded fashion. The details of patients are summarized in Table 1.

Table 1. Details of patient information

Number of patients	100
Age (years)	
Median	52
Range	26–79
Diagnosis	**Number of patients**
Cervical cancer	61
Ia, b	18
IIa, b	32
IIIa, b	11
Ovarian cancer	35
Ia, b	3
IIa, b	8
IIIa, b	24
Endometrial cancer	4
Treatment	**Number of patients**
ABMK	39
Carbo-VP16	29
Carbo-taxol	10
Placebo	61
Carbo-VP16	39
Carbo-taxol	22

ABMK, *Agaricus blazei Murill* Kyowa.

Therapeutic regimen

Patients were treated with either carboplatin (300 mg/m^2) plus VP16 (etoposide, 100 mg/m^2) or carboplatin (300 mg/m^2) plus taxol (175 mg/m^2) every 3 weeks for at least three cycles with or without daily oral consumption of ABMK (three packs/day, one pack per time, obtained from Kyowa Engineering Co., Tokyo, Japan). Subsequently, the patients were bled 1 day before first chemotherapy, and 1 day before second chemotherapy. The patients tested were under primary-line therapy. The activities of NK and lymphokine-activated killer (LAK) cells and the counts of white blood cells (WBCs), lymphocytes, monocytes, CD3$^+$, CD4$^+$, CD8$^+$, CD48$^+$, and CD56$^+$ cells, as well as H_2O_2 production levels of monocytes were analyzed.

The number of immune cells

WBCs, lymphocytes, and monocytes were counted using an instrument, XE-2100 (Sysmex, Kobe, Japan). The counts of CD3$^+$, CD4$^+$, CD8$^+$, CD48$^+$, and CD56$^+$ cells were analyzed by fluorescence-activated cell sorter (FACS) analysis. Fluorescein isothiocyanate (FITC)-labeled monoclonal antibodies specific for human CD3, CD4, CD8, CD48, and CD56 cells were purchased from DiNona (Seoul, South Korea), Immunotech (Westbrook, ME), or Beckman Coulter (Fullerton, CA).

Isolation of peripheral blood mononuclear cells from blood

Peripheral blood mononuclear cells (PBMCs) were obtained by Ficoll–Paque density gradient centrifugation of leukocyte buffy coats, which in turn were obtained from patients at the Kangnam St. Mary's Hospital. The mononuclear cells were washed with phosphate-buffered saline twice which was then used to further purify selected cell population.

NK and LAK cell cytotoxicity assay

NK cells were purified from PBMCs using CD56 microbead (Miltenyi Biotec, GmBH, Bergisch Gladbach, Germany) according to the manufacturer's protocol. The FACS analysis of the purified NK cells showed more than 95% purity. NK cells were then reacted with target cells, K562, at the relative cell count ratio of 20:1 for 4 h at 37 °C. In particular, for LAK activity studies, purified NK cells were first stimulated with recombinant human interleukin-2 (IL-2) (Sigma, St. Louis, MO) at the concentration of 400 U/ml for 24 h. LAK cells were then reacted with target cells, Daudi, at the relative cell count ratio of 3:1 for 3 h at 37 °C. After incubation, cell supernatant was collected and evaluated using cytotoxicity detection kit (BM, Manheim, Germany) according to the manufacturer's protocol. Subsequently, optical density was detected for lactate dehydrogenase activity at 490/630 nm, and then cytotoxicity was calculated as follows:

H_2O_2 assay of monocytes

Monocytes were purified from PBMCs using CD14 microbeads (Miltenyi Biotec) according to the manufacturer's protocol. The FACS analysis of the purified monocytes showed more than 95% purity. Monocytes were then reacted with 50-fold diluted 2′,7′-dichlorofluorescein diacetate (10 μg/ml) solution and incubated for 1 h at 37 °C. After incubation, H_2O_2 production levels in a form of relative fluorescence unit were evaluated by measuring optical density at the wavelength of 485/535 nm using Cytofluorometer (Millipore, Bedford, MA).

Questionnaires

At the time of completion of ABMK treatment, all participants completed a questionnaire that sought data on physical and emotional conditions of the patients. These conditions include insomnia, appetite, alopecia, body weight, nausea/vomiting, emotional conditions, discomfort, and general body strength. QLQ-30 Scoring Manual (2nd edition) of EORTC (European Organization for Research and Treatment of Cancer) was modified and then used in this study as a questionnaire. All questions were given in two parts under three answer conditions (physical status: better, worse, no change; emotional status: no help, helpful, very helpful). This was expressed in percentage.

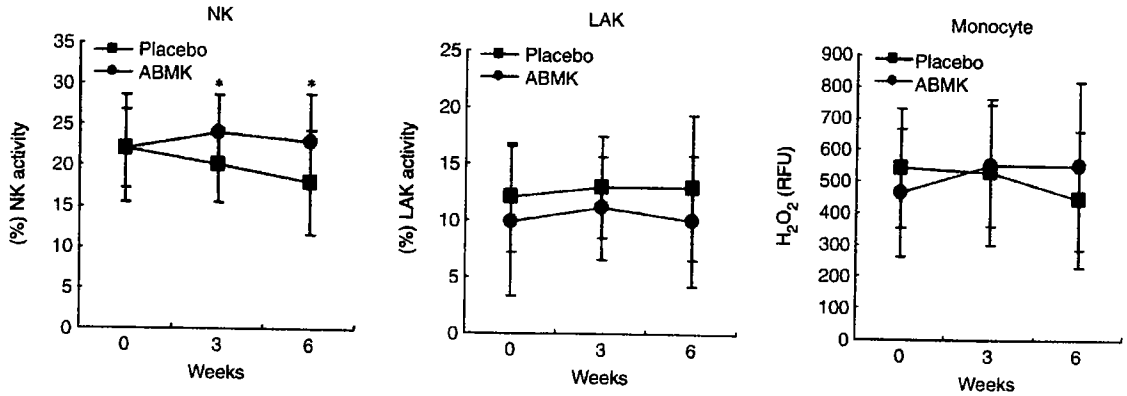

Fig. 1. Natural killer (NK), lymphokine-activated killer (LAK), and monocyte activities of patients undergoing chemotherapy with and without *Agaricus blazei Murill* Kyowa (ABMK) treatment. Gynecological cancer patients were treated with either carboplatin (300 mg/m2) plus VP16 (100 mg/m2) or carboplatin (300 mg/m2) plus taxol (175 mg/m2) at 0, 3, and 6 weeks. ABMK was orally administered every day (three packs/day). One day before each chemotherapy, blood was withdrawn, and the immune cells were tested as shown in Materials and methods. RFU, relative fluorescence unit. *Statistically significant using anova at $P < 0.05$ compared to placebo-treated group.

Results

Gynecological cancer patients were divided into two groups in a double-blind manner. These patients were administered systemically with carboplatin plus VP16 or with carboplatin plus taxol. Among these, one group of patients received ABMK, whereas the other group received placebo. Blood was withdrawn and evaluated for NK cell activity of these patients. As shown in Figure 1, NK cell cytotoxic activity was significantly higher (ANOVA, $P < 0.002$) in ABMK-treated group ($n = 39$) over 3- and 6-week periods, as compared with placebo control group ($n = 61$). However, no difference in NK cell activity was observed before ABMK treatment. This suggests that ABMK consumption might contribute to sustained NK cell cytotoxic activity in gynecological cancer patients undergoing chemotherapy. However, no significant difference was observed in LAK cell cytotoxicity activity between placebo- and ABMK-treated groups over time.

We were also interested in testing monocyte activities of gynecological cancer patients undergoing chemotherapy upon ABMK treatment. We evaluated H_2O_2 production levels of monocytes as an indicator of the monocyte activity. As shown in Figure 1, H_2O_2 production levels were maintained in a similar fashion over the time periods (0, 3, and 6 weeks) following

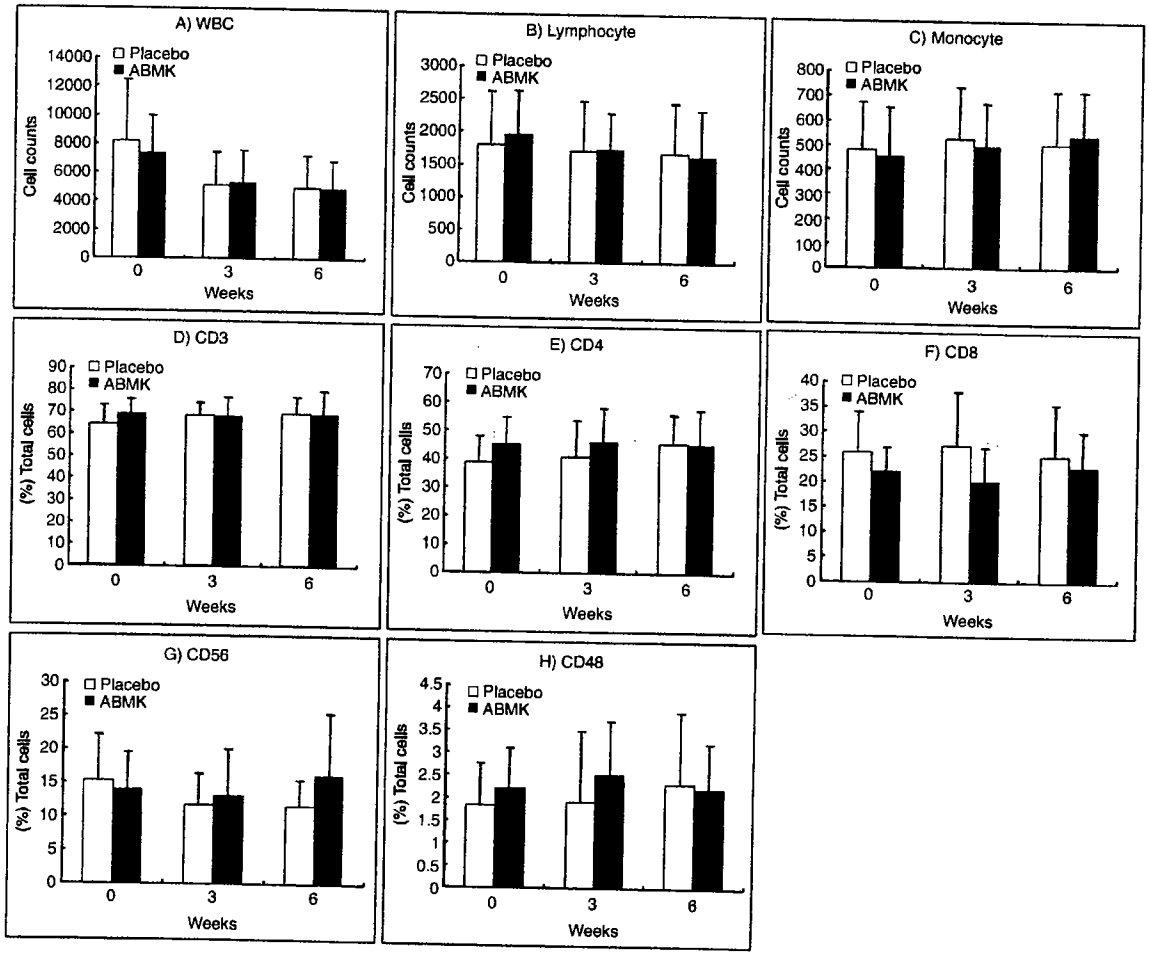

Fig. 2. The cell counts or percent of white blood cells (WBCs) (A), lymphocytes (B), monocytes (C), and specific cell population (D–H) in patients undergoing chemotherapy with and without *Agaricus blazei Murill* Kyowa (ABMK) treatment. Gynecological cancer patients were treated with either carboplatin (300 mg/m^2) plus VP16 (100 mg/m^2) or carboplatin (300 mg/m^2) plus taxol (175 mg/m^2) at 0, 3, and 6 weeks. ABMK was orally administered every day (three packs/day). One day before each chemotherapy, blood was withdrawn, and the immune cells were tested as shown in the Materials and methods.

chemotherapy with or without ABMK consumption. Furthermore, no significant difference in the monocyte activity was observed between placebo- and ABMK-treated groups.

To determine whether ABMK consumption might influence immune cell populations in patients undergoing chemotherapy, we next counted the specific immune cell populations, such as WBCs, lymphocytes, monocytes, $CD3^+$, $CD4^+$, $CD8^+$, $CD48^+$, and $CD56^+$ cells. As shown in Figure 2A, upon chemotherapy, a decrease in the WBC count was detected. However, no increase in the WBC count was detected after ABMK consumption. Furthermore, no significant difference in the counts of cells including lymphocytes, monocytes, T cells, $CD48^+$ cells, and $CD56^+$ cells was observed between placebo- and ABMK-treated cancer patient groups (Fig. 2B–H).

By questionnaires, we also evaluated physical and emotional conditions of patients undergoing chemotherapy with or without ABMK consumption. In this study, we focused solely on any benefits of ABMK treatments in contrast to placebo treatments in patients under chemotherapy. The data on insomnia, appetite, alopecia, body weight, nausea/vomiting, emotional conditions, discomfort, and general body strength were collected. As shown in Figure 3, these physical and mental conditions, in particular appetite, alopecia, nausea/vomiting, emotional conditions, and general body strength improved significantly after ABMK consumption, as compared with placebo consumption, suggesting a positive effect of ABMK consumption on the patients' overall conditions.

Discussion

Studies in many experimental animal models have demonstrated that a variety of natural fungal products have antitumor activities[13–15]. In particular, intratumoral injection or oral administration of *A. blazei* extracts results in tumor regression[16]. In the same study, the antitumor efficacy was improved in particular when *A. blazei* extracts were treated with acids, suggesting an importance of the chemical state of *A. blazei* extracts. We also observed that NK cell activity was maintained to a more significant level in the gynecological cancer patient groups undergoing chemotherapy when ABMK was orally consumed. This suggests that ABMK might have some beneficial effects on innate immunity in gynecological cancer patients undergoing chemotherapy. This is also in line with preclinical reports that treatment with *A. blazei* extracts results in more infiltration of NK cells in the tumor sites and more increased NK cell activity[7,12]. NK cells play an important role in the innate immunity by recognizing major histocompatibility class I-negative target cells, which can escape immune surveillance by cytotoxic T cells. NK cells display dramatic effects on the reduction of tumor growth as well as on the inhibition of metastatic tumors[17]. The mechanism(s) of controlling NK cell cytotoxicity are gradually being elucidated but still remain fragmentary. In addition to direct lysis of target cells, NK cells express CD16, which allows for their participation in antibody-dependent cell cytotoxicity of immunoglobulin-coated tumor cells. It has also been reported

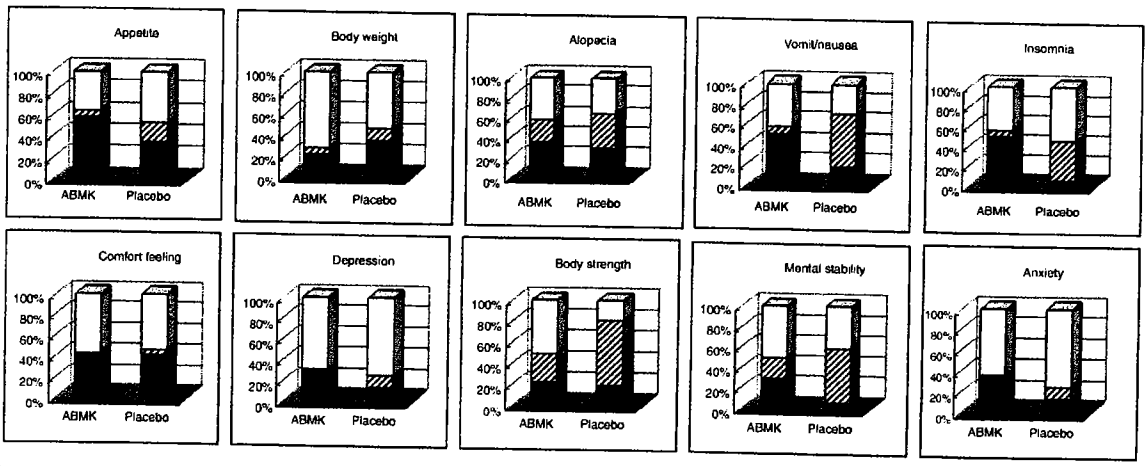

Fig. 3. Evaluation of qualities of life in patients undergoing chemotherapy with and without *Agaricus blazei Murill* Kyowa (ABMK) treatment. Gynecological cancer patients were treated with either carboplatin (300 mg/m^2) plus VP16 (100 mg/m^2) or carboplatin (300 mg/m^2) plus taxol (175 mg/m^2) at 0, 3, and 6 weeks. ABMK was orally administered every day (three packs/day). At the time of completion of treatment, the patients were asked to fill out questionnaires to evaluate their own physical and mental conditions. ■, improved; ▨, worsened; □, no change.

that direct intratumoral injection of ABMK can induce apoptosis and cell-cycle arrests of tumor cells[12]. Based on this, ABMK appears to be beneficial for cancer patients. Similarly, *A. blazei Murill* extracts can stimulate macrophages and then induce the secretion of tumor necrosis factor-α, IL-8, and nitric oxide[18]. This further supports the possible benefits of ABMK. We also investigated whether ABMK consumption might influence general physical and mental conditions of gynecological cancer patients undergoing chemotherapy. We observed that the ABMK consumption reduced some chemotherapy-related side effects in patients. In general, insomnia, appetite, alopecia, body weight, nausea/vomiting, emotional conditions, discomfort, and general body strength were all improved, indicating that ABMK consumption could be one effective approach to reduce some chemotherapy-associated side effects. It could be suspected that chemotherapeutic drugs might interact with ABMK extracts and then decrease the efficacy of chemotherapeutic drugs in the patients. However, it is unlikely that chemotherapeutic drugs administered intravenously can interact directly with any components of ABMK extracts fed orally. However, this needs further investigation for any possible complications.

Taken together, oral delivery of ABMK provides an additional alternative therapeutic modality to maintain innate NK cell activity and, in particular, reduce many severe side effects caused by chemotherapy in gynecological cancer patients.

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COMPLAINT COUNSEL'S EXHIBIT 5

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Domain Name Expiration Notice

Call us toll free at 1-866-434-0212 24 hours a day
or visit us at www.drea.com

Domain Name(s): agaricus.net
opc-agaricus.net
etsc-euskirchen.com

Reply Requested By: February 22, 2008

As a courtesy to domain name holders, we are sending you this notification of the domain name registrations that are du to expire in the next few months. When you switch today to the Domain Registry of America, you can take advantage c our best savings. Your domain name registrations will expire in June 2008. Act today!

You must renew your domain name to retain exclusive rights to it on the Web, and now is the time to transfer and renev your names from your current Registrar to the Domain Registry of America. Failure to renew your domain name by th expiration date may result in a loss of your online identity making it difficult for your customers and friends to locate you o the Web.

Privatization of Domain Registrations and Renewals now allows the consumer the choice of Registrars when initiall registering and also when renewing a domain name. Domain name holders are not obligated to renew their domain name with their current Registrar or with the Domain Registry of America. Review our prices and decide for yourself. You are under no obligation to pay the amounts stated below, unless you accept this offer. **This notice is not a bill**, it is rather a easy means of payment should you decide to switch your domain name registration to the Domain Registry of America.

Term	Period Covered	Price
1 year	Until - June 2009	**$30.00**
2 years (Recommended)	Until - June 2010	**$50.00** (save $10)
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The following names are currently available for you to register and secure, protecting your domain name from being duplicated.

Other Available Domains	Period Covered	Price
there are no other extensions of your domain name currently available.		
there are no other extensions of your domain name currently available.		
opc-agaricus.com	2 Years	$50.00 (save $10)
opc-agaricus.org	2 Years	$50.00 (save $10)
etsc-euskirchen.net	2 Years	$50.00 (save $10)
etsc-euskirchen.org	2 Years	$50.00 (save $10)

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1 Year	$30.00	☐
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2 Year	$50.00	☐
5 Year	$95.00	☐

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2 Year	$50.00	☐
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