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

In the Matter of	)	
DANIEL CHAPTER ONE,	)	
a corporation, and	)	**Docket No. 9329**
JAMES FEIJO,	)	**Public Document**
individually, and as an officer of	)	
Daniel Chapter One	)	

EXHIBITS SUBMITTED IN SUPPORT OF COMPLAINT COUNSEL'S MOTION FOR SUMMARY DECISION - VOLUME I

Complaint Counsel submit the following exhibits referenced in the Statement of Material Facts As To Which There is No Genuine Issue (the "Statement of Facts") and are separately submitting a bound copy of the deposition testimony taken in this case and referenced in the Statement of Facts.

1. Declaration of Complaint Counsel's Expert Denis R. Miller, M.D., dated February 18, 2009, attaching Expert Report, dated January 28, 2009

2. Declaration of Complaint Counsel Theodore Zang, Jr., dated February 23, 2009

3. Declaration of FTC Investigator Michael Marino, dated February 23, 2009, and Exhibits A - N thereto

4. Deposition of Respondent James D. Feijo Exhibit 7 - Respondents' Responses to Complaint Counsel's First Set of Interrogatories

5. Deposition of Respondent James D. Feijo Exhibit 12 - BioGuide: The BioMolecular Nutrition Guide to Natural Health 3 [FTC-DCO 0306 - 0381]

6. Deposition of Respondent James D. Feijo Exhibit 6 - BioMolecular Nutrition Product Catalog [FTC-DCO 0060 - 0063]

7. Deposition of Respondent James D. Feijo Exhibit 4 - Exhibits A - D to Administrative Complaint [FTC-DCO 0011 - 0032]

8. Respondents' Responses and Objections to Complaint Counsel's Request for Admissions, dated December 29, 2008

9. Deposition of Respondent James D. Feijo Exhibit 9 - Daniel Chapter One Monthly Gross Sales

10. Daniel Chapter One's Cancer Newsletter, Millenium [sic] Edition, 2002 - "How to Fight Cancer is Your Choice!!!" [FTC-DCO 0390 - 0405]

11. Pages from Respondents' Web site dc1store.com listing contact information, dated March 31, 2008 [FTC-DCO 0083 - 0086]

12. Pages from Respondents' Web site dc1store.com discussing "DC1 Affiliate Program," dated December 12, 2007 [FTC-DCO 0461 - 0463]

13. Terry Brotherton Statement produced by Respondents as DCO 0156

14. Charlotte Rice Statement produced by Respondents as DCO 0170 - 0171

15. Earl Davis Statement produced by Respondents as DCO 0187

16. Ernie Jenson Statement produced by Respondents as DCO 0189 - 0193

17. Pages from Respondents' Web sites dc1pages.com, dated April 2, 2008, [FTC-DCO 0159 - 0161] and danielchapterone.com, dated November 7, 2008, [FTC-DCO0493 - 0496] stating "I think it costs too much"

18. Deposition of Patricia Feijo Exhibit 14 - Bio*Shark Labels [FTC-DCO 0065 - 0066, 0122 - 0123]

19. Deposition of Patricia Feijo Exhibit 15 - 7 Herb Formula Labels [FTC-DCO 0064, 0124]

20. Deposition of Patricia Feijo Exhibit 16 - GDU Caps Labels [FTC-DCO 0125 - 0126, 0067 - 0068]

21. Deposition of Patricia Feijo Exhibit 17 - BioMixx Labels [FTC-DCO 0127 - 0128]

22. Pages from Respondents' Web site dc1pages.com regarding "Supporting Products," dated April 2, 2008 [FTC-DCO 0186 - 0192]

23. Testimonials from Respondents' Web site [FTC-DCO 0100 - 0119]

24. Respondents' "Web Pages from prior Daniel Chapter One Web sites" [FTC-DCO 2030 - 2041]

25. Pages from Respondents' Web sites dc1pages.com, dated April 2, 2008, [FTC-DCO 0140 - 0143] and danielchapterone.com, dated November 7, 2008 [FTC-DCO 0493 - 0496] regarding "I want the Original Essiac Formula, not some knock off brand"

26. Pages from Respondents' Web site dc1pages.com regarding "I use Brand X," dated April 2, 2008 [FTC-DCO 0157 - 0158]

27. Respondents' Responses to Complaint Counsel's First Request for Production of Documentary Materials and Tangible Things, dated December 8, 2008

Respectfully submitted,

David W. Dulabon

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Federal Trade Commission
Alexander Hamilton U.S. Custom House
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Dated: February 24, 2009

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on February 24, 2009, I have filed and served the attached **COMPLAINT COUNSEL'S STATEMENT OF MATERIAL FACTS AS TO WHICH THERE IS NO GENUINE ISSUE,** and all documents and depositions cited therein as set forth below:

The original and one paper copy via overnight delivery and one electronic copy via email, and one bound copy of all documents and depositions cited herein, to:

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

Two paper copies via overnight delivery, and one bound copy of all documents and depositions cited herein, to:

The Honorable D. Michael Chappell
Administrative Law Judge
600 Pennsylvania Ave., N.W., Room H-528
Washington, DC 20580

One electronic copy via email and one paper copy via overnight delivery, and one bound copy of all documents and depositions cited herein, to:

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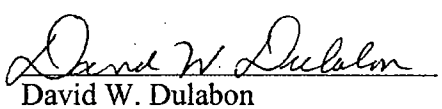

David W. Dulabon
Complaint Counsel

Declaration of Denis R. Miller, M.D.
Pursuant to 28 U.S.C. § 1746

I, Denis R. Miller, M.D., declares under penalty of perjury as follows:

1. I have been retained by the Federal Trade Commission ("Commission") as an expert witness in the Commission's action against Daniel Chapter One and James Feijo. As part of my duties as an expert witness in this matter, I prepared a report detailing my findings about the Daniel Chapter One's products which are the subject of the Commission's action. A true and correct copy of the expert report that I prepared in this case, is attached to this declaration as Exhibit A.
2. I declare under penalty of perjury that the foregoing is true and correct.

Executed February 18, 2009

Denis R. Miller, M.D.

EXPERT REPORT OF DENIS R. MILLER, MD

I. QUALIFICATIONS

As detailed in my curriculum vitae, I am a board certified pediatric hematologist/oncologist and am licensed to practice medicine in the State of New Jersey. Currently, I am on the voluntary faculty (Clinical Professor of Pediatrics) at Robert Wood Johnson School of Medicine (New Brunswick, NJ).

For over 40 years I directed clinical care, education, laboratory and clinical research, and administration, heading divisions or departments at University of Rochester Medical Center, New York Hospital-Cornell Medical Center, Memorial Sloan Kettering Cancer Center (MSKCC), and Northwestern University Medical School (Chicago, IL). My major area of clinical and laboratory research was hematopoietic malignancies. I was the recipient of research grants from the National Cancer Institute, private foundations, and other organizations. As Chairman of the Department of Pediatrics at MSKCC, I directed one of the largest pediatric oncology/hematology programs in the world and held an endowed chair. Our department was heavily involved in more than 25 Phase I studies annually. Many of these investigational agents are now cornerstones in cancer treatment.

From 1990 to 1996, I served as Associate Medical Director of Cancer Treatment Centers of America (CTCA) and from 1993 to 1996 I was the Scientific Director of CTCA's Cancer Treatment Research Foundation (CTRF). In both capacities, I was involved actively in designing clinical research protocols for patients with a wide variety of malignancies. In my capacity as Scientific Director, I supervised the clinical research program, chaired the Scientific Advisory Committee of the Institutional Review Board, and was principal investigator for a number of Phase I/II studies. These studies included

innovative treatment for cancers of the head and neck, lung, breast, pancreas, and colon as well as hematological malignancies and other disorders. These new agents included antiangiogenic compounds, immunomodulators, differentiating drugs, inducers of apoptosis, and monoclonal antibodies directed against tumor-specific antigens.

I understand and respect the position and role of supportive care and complementary medicine in oncology and how they blend with conventional therapy. I conducted studies on Maitake mushroom and panax ginseng in patients with cancer. I also directed a Phase I/II randomized, open-label, single institution study of a commercially-available shark cartilage product (Cartilade®). A more detailed review of the design and results (Miller, et al, 1998) of this study will be presented in my review of the Daniel Chapter One (DCO) product known as Bio*Shark.

I have performed numerous studies in early (Phase I) and later clinical development (Phase II through Phase IV). I worked on differentiating and apoptosis-inducing agents (histone deacetylase inhibitors), monoclonal antibodies (rituximab, trastuzumab), small molecule epidermal growth factor receptor inhibitors (gefitinib), cyclin dependent kinase inhibitors (flavopiridol), and erythropoietic stimulating agents (epoetins alfa and beta). Specific tumor types included acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL), non-small cell lung cancer (NSCLC), mesothelioma, CRC, and cancers of the head and neck, esophagus, pancreas, breast, and skin (malignant melanoma).

Currently, I am the Oncology/Hematology Therapeutic Area Leader at PAREXEL International, one of the world's leading contract research organizations (CRO). CROs manage clinical trials for the pharmaceutical industry and are involved in the entire

process of testing and evaluating new agents through the various phases of clinical development. The ultimate goal is to make these new agents available to cancer patients and improve their survival and quality of life. As such, I am fully familiar with good clinical practice requirements, study design and conduct, regulatory requirements for each phase of clinical development, biostatistical considerations that demonstrate efficacy and safety, the role of supportive care in cancer drug development, informed consent, and regulatory guidelines for alternative and complementary treatments in patients with cancer and blood diseases. Because of potential drug-drug interactions, I am acutely aware of safety issues associated with the use of any anticancer agent and the use of concomitant drugs that might potentially increase a patient's risk of having adverse reactions (toxicity or "side effects") or decrease the efficacy of other required medications. These data are obtained in the early phases of drug development and is a major objective of Phase I/II.

I am a member of ASCO, AACR, and ASH and served on the editorial boards of the British Journal of Haematology and the American Journal of Clinical Oncology (Associate Editor, Pediatric Oncology). I have authored or co-authored over 300 book chapters, peer-reviewed articles, and abstracts. I was senior editor to 4 editions of a classic textbook in pediatric hematology/oncology, *Blood Diseases of Infancy and Childhood*

In summary, for the past 43 years (since 1966), I have been actively engaged in the design, implementation, completion, regulatory review, analysis, presentation, publication, and when appropriate, regulatory approval worldwide of many anticancer agents that were evaluated in studies designed to make these agents available to patients.

I am familiar with the pharmacology (pharmacokinetics, pharmacodynamics), mechanism(s) of action, safety, and therapeutic efficacy, including clinical benefit, of

drugs and other anticancer agents. I also understand the importance of formulation in cancer drug development. By definition, formulation is the process of adding all of the ingredients in a product, including specific concentrations of each of the active agents, excipients, stabilizers, solubilizers, flavoring, and colorizers, and determining whether the product will be in capsule, tablet, or liquid form. I am familiar with drugs and other agents as well as their formulations, doses, and dose schedules that are generally recognized by experts as safe and effective for human use in specific indications. This knowledge comes from a professional life devoted to my patients and my involvement in the process of clinical drug development.

Thus, based on my training, experience, and ongoing clinical activities, I am well qualified to offer my expert opinion in this case.

II. SCOPE OF WORK

I have been asked by the FTC to determine whether there is competent and reliable scientific evidence to substantiate the following claims:

- Bio*Shark inhibits tumor growth;
- Bio*Shark is effective in the treatment of cancer;
- 7 Herb Formula is effective in the treatment or cure of cancer;
- 7 Herb Formula inhibits tumor formation;
- GDU eliminates tumors;
- GDU is effective in the treatment of cancer;
- BioMixx is effective in the treatment of cancer; and
- BioMixx heals the destructive effects of radiation and chemotherapy.

Compensation: $250/hour.

Prior Expert Testimony: A listing for the past 4 years is in APPENDIX I.

III. MATERIALS CONSIDERED

To form my opinion, in addition to drawing upon my extensive expertise in cancer care and treatment, I have conducted literature searches as follows:

- PubMed, Google, PDQ, NCI, MSKCC, MD Anderson Cancer Center, Dana Farber Cancer Institute, Search Medica, Stanford HighWire, Clinical Trials.gov, many cancer and hematology journals (e.g. Journal of Clinical Oncology, Clinical Cancer Research, Blood, British Journal of Haematology, Supportive Care in Oncology, American Journal of Oncology, New England Journal of Medicine, etc.) (APPENDIX III)

I have also reviewed the following material provided to me by the FTC:

- Official Transcripts of DCO Healthwatch Radio Program on Accent Radio Network, July 8, 2008, and July 14, 2008
- Testimonials submitted by 30 patients who used DCO products
- Respondents' Responses to Complaint Counsel's First Set of Interrogatories
- Daniel Chapter One Product Labels (for products for which representations have been made regarding cancers or tumors)
- BioGuide, the Biomolecular Guide for Daniel Chapter One
- Literature provided by DCO:
    - Articles for Research Study of Complimentary/Alternative Proprietary Products in Support of Respondent's Claims (Appendix III)
    - Other cited articles:
        - Lane IW, Comac L. Sharks Don't Get Cancer. How Shark Cartilage Could Save Your Life. 1993.
        - Dr. Nieper's Revolution in Technology Medicine and Society, 1985

- Blumenthal M, Goldberg A, Brinckmann J, et al. Herb Medicine, Expanded Commission E Monographs,
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- Naturopathic Handbook of Herb Formulas, 4th Ed, 1995, Herb Research Publications, Inc. Ayer, MA.(Cover/Title pages only
- Mindell E. Earl Mindell's Secret Remedies, 1997, Fireside Press, New York, NY (Cover/Title pages only

- Tenney L. Today's Herb Health, 3rd Ed, 1992, Woodland Books, Provo, UT.(Title/pages only)
- Miscellaneous Title/Cover pages only of The Vitamin Herb Guide, Treatment for the World's 160 Most Common Ailments, Weiner's Herb, The Guide to Herb Medicine (1990),

- Respondents' Expert Witness Disclosure
- Administrative Complaint of Federal Trade Commission
- Administrative Complaint, Exhibits A-D (re Bio*Shark, GDU, 7 Herb Formula, BioMixx)
- Guidance for Industry on Complementary and Alternative Medicine Products and Their Regulation by the Food and Drug Administration, December 2006.
- Daniel Chapter One Medical Sources for Alleged Deceptive Statements
- Relevant medical literature on efficacy and safety of components of DCO products (Bio*Shark, GDU, 7 Herb Formula, BioMixx)
- Marketing information on DCO products from www.danielchapterone.com
- Deposition Testimony, James Feijo, January 13, 2009
- Deposition Testimony, Patricia Feijo, January 14, 2009

IV. SUMMARY OF OPINIONS

Based upon my professional training and experience and my review of all of the materials cited above, it is my opinion that there is no competent and reliable scientific evidence to substantiate the claims that the products at issue treat, cure, and prevent cancer.

V. WHAT CONSTITUTES COMPETENT AND RELIABLE SCIENTIFIC EVIDENCE

Based on my extensive experience in academic medicine from 1966 to 1996 and in the pharmaceutical industry from 1997 until today, it is my opinion that to constitute competent and reliable scientific evidence, a product that purports to treat, cure, or prevent cancer must have its efficacy and safety demonstrated through controlled clinical studies.

My understanding of what constitutes competent and reliable scientific evidence is consistent with the FDA's regulations that define the criteria for adequate and well-controlled clinical investigations, which are set forth at 21 C.F.R Sec. 314.126. My understanding also is coonsiteent with the guidelines set forth by FDA entitled "Guidance for Industry on Complementary and Alternative Medicine Products and Their Regulation by the Food and Drug Administration, (October 2006)."

The proper format for any clinical trial protocol includes the following:

1) details of the **rationale** for the study relating the critical features (aims, target population, design, treatment, dosage, route of administration, duration, and primary endpoints) to the development of the investigational drug;

2) clear elucidation of **primary and secondary objectives**;

3) clear presentation of the **investigational plan,** including a) **study design**, including number of centers, type of study (e.g. open label or double-blind), randomization with or without stratification, duration of each study phase, total duration of study, treatment groups, special features, special subsets, and effects of interim analysis on power of study, if planned; b) **selection of subjects** including number, inclusion and exclusion criteria; c) **study treatments,** including dosage schedule, treatment assignment, randomization schedule, blinding/packaging/labeling, mechanisms to ensure compliance; d) documentation of **prior and concomitant illnesses and treatments;** and e) **study procedures and schedules** (for evaluation of safety and efficacy).

4) complete overview and description of specific methods of **data collection**, quality assurance, and quality control;

5) complete description of all **statistical procedures**;

6) if relevant, full reporting of results of studies of **pharmacokinetics, pharmacodynamics, quality of life, and health economics;**

7) complete and concise discussion of **overall conclusion** regarding safety and efficacy;

8) relevant **references**;

9) accompanying **Tables and Figures;**

10) selected **subject listings** of demographics, disease and treatment parameters, endpoints, safety factors, and deaths); and

11) subject narratives for serious adverse events and deaths.

Clinical drug development is a complicated, lengthy, and expensive process. Of any 5000 promising agents discovered in the laboratory and entering nonclinical testing, 5 enter Phase I and one is approved. Nonclinical studies are performed in the test tube and in animals with the aim of demonstrating potential activity and acceptable safety in animals. Once nonclinical studies have been performed, a new agent enters Phase I "first in humans" clinical trials. In oncology, previously treated cancer patients are usually enrolled in these Phase I studies. A Phase I study is designed to determine the pharmacokinetics, pharmacodynamics, maximal tolerated dose, dose limiting toxicity, safety, and recommended Phase II dose of the candidate new agent. In the next step, Phase II, the efficacy and safety of the new agent is evaluated in selected cancers and targeted patient populations. The last step is the performance of randomized, controlled Phase III clinical trials. The decision to proceed to Phase III is generally based on the justification for the dose/dose regimen, on the robustness of the efficacy data, and the assurance of an acceptable safety profile derived from the Phase II studies. A successful

Phase III study meets its predefined endpoints with statistical robustness and with an acceptable safety profile.

Determining the mechanism of action of a new agent to treat cancer is a critical aspect of cancer drug development. Anticancer agents may work by preventing cell proliferation (division), induce programmed cell death (apoptosis), inhibit growth factors or biochemical pathways that result in cell death, and important in this matter, inhibition of new blood vessel formation or angiogenesis.

Angiogenesis is an important and vital mechanism of tumor growth and metastasis. Antiangiogenic agents have an important role in the treatment of some types of cancer. During the past 9 years I have been involved in the development of a number of antiangiogenic agents, some of which are undergoing early stages of development and others are now approved to treat cancer. All of these approved antiangiogenic compounds underwent Phase I/II/III studies and have been the subject of scientific presentations and publications. These antiangiogenic agents are now being used with chemotherapy to treat a variety of solid tumors and hematologic malignancies.

Most of these antiangiogenic agents are highly purified, synthesized products, recombinant molecules, or humanized monoclonal antibodies with known mechanisms of action. They have well-characterized pharmacokinetics, pharmacodynamics, and dose/dose schedules. As targeted therapies, they have a different safety profile than conventional chemotherapy. Unlike crude raw materials, all have known targets regarding their active antiangiogenic activity.

Many of the studies cited by DCO in support of their position and provided to me by the FTC are nonclinical (in vitro or in animals). Other reported studies have evaluated

isolated compounds that are also present in certain DCO products. Some of these individual compounds showed nonspecific immunostimulatory activities or suggested cancer preventive effects. However, nonclinical studies can not replace the actual evaluation of DCO products themselves. Each DCO product or active ingredient must be subjected to the same experimental conditions to demonstrate anticancer activity. It is not possible to extrapolate from the results of a published nonclinical study of curcumin for example and state that GDU can eliminate tumors.

Complementary medicine's role is not to replace conventional anticancer therapy. Complementary medicine adds to the efficacy of standard anticancer therapy, reducing some of cancer therapy's adverse side effects (e.g. nausea and vomiting, severe neutropenia, anemia, fatigue), improving general well-being and quality of life, and permitting oncologists to administer effective doses of therapy on time. It is well known that many new targeted therapies work better when given with conventional anticancer therapy and rarely are as efficacious when given as single agents. Similarly, complementary medicine should and does not serve as an alternative to effective and safe anticancer therapy. Suggesting that it can be an effective substitute for traditional medicine would be a diservice to cancer patients. Delays in effective therapy may allow cancer cells to regrow, develop resistance to therapy, and metastasize.

Anecdotal reports of a drug's efficacy conducted outside the setting of a controlled clinical trial do not replace clinical trials that are designed to demonstrate safety and efficacy. Without confirmation of the diagnosis of cancer, predefined strict eligibility criteria, a rational and justified dosing schedule, safety monitoring, and carefully defined endpoints, anecdotal reports are not reliable and competent, lack statistical robustness, are

short on scientific quality or validity and can never substitute for a well-designed and well-conducted controlled clinical trial. Anecdotal reports represent the weakest form of evidence supporting the anticancer activity of a new agent. I am unaware that anecdotal reports provided adequate evidence to provide the basis for regulatory approval of any new anticancer agent.

As I will review, not only are there no peer-reviewed data to demonstrate a role for any DCO product in the treatment of human cancer, but also, the use of these products presents a potential harm. This is most acute if a cancer patient foregoes potentially beneficial and effective therapy and replaces that option with Bio*Shark, GDU, 7 Herb Formula, or BioMixx, alone or in combination with other DCO products. Diagnosing cancer early and treating it appropriately and effectively still offers the best chance of curing it. The use of complementary or alternative therapies exclusively as front-line (first) treatment will surely result in disease progression and death.

The risks of untested and unregulated remedies were succinctly stated by Angell and Kassirer in an editorial published in the New England Journal of Medicine in 1998:

> "It is time for the scientific community to stop giving alternative medicine a free ride. There cannot be two kinds of medicine—conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work. Once a treatment has been tested rigorously, it no longer matters whether it was considered alternative at the outset. If it is found to be reasonably safe and effective, it will be accepted. But assertions, speculations, and testimonials do not substitute for evidence. Alternative treatments should be subjected to scientific testing no less rigorous than that required for conventional treatments."

VI. DETAILED DISCUSSION OF FINDINGS

a. Bio*Shark

The key questions relating to Bio*Shark are:

- Does Bio*Shark inhibit tumor growth?

- Is Bio*Shark effective in the treatment of cancer?

Conclusion:

A thorough review of peer-reviewed literature and of all of the documents produced by DCO indicates that there is no competent and reliable scientific evidence that Bio*Shark inhibits tumor growth in humans or that it is effective in the treatment of cancer in humans.

Discussion

DCO cites 9 nonclinical and 1 clinical studies in support of the clinical efficacy of Bio*Shark, but Bio*Shark was not evaluated in any of them. In the absence of any nonclinical or clinical data on Bio*Shark, it appears that DCO considers any proprietary shark cartilage product as a surrogate for Bio*Shark. Such an assumption is not acceptable scientifically.

A number of reported nonclinical studies suggested that highly purified peptides isolated from shark cartilage may have antitumor activity and antiangiogenic activity. Common in all of these reports was a clear description of the experimental design that included concentration of the peptide being evaluated for its anticancer activity. The nonclinical studies of various, mostly partially purified isolates from shark cartilage suggested a number of effects including:

- Enhanced immune response and decreased tumor size in animals treated intraperitoneally (injected into the abdominal cavity).
- Inhibition of angiogenesis in rabbit cornea.
- Inhibition of endothelial cell function and decreased vascular endothelial growth factor (an important angiogenic factor) production in cancer cells.
- Inhibition of growth of lung carcinoma growth.

Three nonclinical *in vivo* studies of orally-administered crude shark cartilage have been published in the peer-reviewed literature. (PDQ, NCI, April 2008). In one study, an unidentified shark cartilage product inhibited chemically-induced angiogenesis in rats. In

a second study, shark cartilage (unknown brand) inhibited the growth of gliosarcoma in rats. In a third study, two other shark cartilage products (Sharkilage, MIA Shark Powder) did not inhibit the growth or metastasis of squamous cell carcinoma in mice. Thus, even the nonclinical efficacy data regarding orally administered shark cartilage are inconclusive.

The take home message from the nonclinical studies is that evidence of antitumor, antiangiogenic, and immunostimulatory activity in vitro or in animal models using ***highly purified peptides*** from shark cartilage administered parenterally (not by mouth) or shark cartilage powder administered orally does not translate to anticancer activity of crude shark cartilage given to human cancer patients. Specific amounts of antiangiogenic peptides were administered to animals or inserted in Petri dishes with tumor cells or endothelial cells to measure activity. Entirely unknown is the amount of functionally active antiangiogenic peptides or other anticancer compounds that are absorbed after oral administration of crude or aqueous extracts of shark cartilage in humans.

The DCO recommended dose is "2-3 800 mg capsules three times a day." The calculated daily dose is 4.8 – 7.2 g/day. Most clinical trials of crude or partially purified shark cartilage used a dose of 1 g/kg/day. Thus, even if shark cartilage were active, the dose recommended by DCO is about 10% of that given to cancer patients enrolled in clinical trials. This would imply that Bio*Shark is 10 times more potent with respect to antiangiogenic activity than other commercially available products. Comparative bioavailability/bioequivalence studies of the different commercially available products and nonclinical studies to evaluate antiangiogenic and other alleged activities of shark cartilage are needed to establish an appropriate safe and effective dose in humans. These studies have not been done.

Are there any reliable scientific data supporting a role of orally-administered shark cartilage in treating patients with cancer? NCI/PDQ in April 2008 updated the current status of the use of shark cartilage in the treatment of cancer and summarized data from 8 clinical studies that had predefined clinical endpoints (Table 1).

Table 1. Summary of Clinical Trials of Shark Cartilage

Reference^	Phase	Cancer Indication	Cartilage Product (Source)	N	Best Response	Concurrent Therapy	Level of Evidence*
Prudden et al, 1995	Case Studies	Advanced, metastatic	Catrix (bovine)	31	CR-19	Yes	3iiiDiii
Romano et Al, 1985	II	Metastatic	Catrix (bovine)	9	CR-1 (RCC)	No	3iiiDiii
Puccio, 1994	II	Metastatic renal cell	Catrix (bovine)	35	PR-3/22 evaluable	Unknown	None
Falandreau, et al, 2001 Batist, et Al, 2002]	I/II	advanced, refractory solid tumors	AE-941/ Neovastat (shark)	331	↑ OS (NSCLC-Unplanned) RCC (planned)	Unknown	None
Latreille et Al, 2002	I/III	IIIB/IV NSCLC	AT-941/ Neovastat (shark)	80	No DLT ↑ OS @ ↑ doses No tumor Responses	Yes or refused standard therapy	None
Miller et al, 1998	I/II	Advanced solid tumors	Cartilade (shark)	60	SD (12 wk). 10/50	No	3iiiDiii
Leitner, et Al, 1998	II	Metastatic refractory breast	Unknown (shark)	20	SD (12 wk). 2/10	No	None
Leitner et al, 1998]	II	Metastatic, prostate	Unknown (shark)	12	SD (20 wk). 3/10	No	None
Rosenbluth et al, 1999	II	advanced brain	BeneFin (shark)	12	SD (20 wk). 2/10	No	None
Loprinzi, et al, 2005	III PC,DB	Breast, colorectal	BeneFin (shark)	42	No statistically Significant Difference	No	1i

^ Full references in APPENDIX II, Bio*Shark

*For information about Levels of Evidence analysis and an explanation of the level of evidence scores, see Levels of Evidence for Human Studies of Cancer Complementary and Alternative Medicine.

Not included in the above review was a subsequent randomized, double-blind, placebo-controlled study of Neovastat (AE-941) in Stage 3 inoperable NSCLC treated with standard induction chemotherapy and chemoradiation therapy. AE-941 did not improve overall survival when compared with placebo. (Lu et al, 2007) The development of Neovastat in cancer has been discontinued.

In summarizing these data in 2008, NCI concluded: "Although at least a dozen clinical studies of cartilage as a treatment for cancer have been conducted since the early 1970s, relatively few results have been reported in the peer-reviewed scientific literature. At present, the use of cartilage (bovine [cow] or shark) as a treatment for cancer cannot be recommended outside the context of well-designed clinical trials."

A number of anecdotal reports of the safety and efficacy of shark cartilage (Cartilade™, BeneFin™, others) have been published in non-peer reviewed journals, presented on television, or have not conformed to good clinical practice required in Phase II or Phase III trials. These anecdotal studies do not provide any competent and reliable scientific evidence to substantiate the claims mentioned above concerning Bio*Shark. (Lane and Contreras, J Naturopath Med 1992; Menendez Lopez, JR et al, 1996; Milner, 1996). In some anecdotes, patients received conventional anticancer therapy followed by shark cartilage. However, shark cartilage was credited for the salutary effects. In summary, these anecdotal reports provide no scientifically useful, competent, valid, or reliable evidence about the efficacy or safety of shark cartilage in patients with cancer.

DCO relies on the work of Dr. I. William Lane of "Sharks Don't Get Cancer" fame. However, Dr. Lane's premise is false as careful studies at Johns Hopkins University indicate that indeed sharks do get cancer (Ostrander, et al, 2004). Ostrander et al provide details on more than 40 examples of tumors in sharks and related species.

Bio*Shark not only contains shark cartilage but also contains 50 mg of "Biomolecular Base". In addition to a number of herbal ingredients (e.g. eleuthero root, garlic, and dandelion), BioMolecular Base contains unspecified amounts of interesting elements and minerals such as barium, bismuth, gallium, silicon, silver, strontium, titanium, vanadium,

and zirconium. I have searched the literature and am unable to find reliable and competent evidence from controlled clinical trials showing any nutritional value of or daily requirement for any of these constituents in Bio*Shark (and GDU).

There are no adequate and well-controlled studies demonstrating that Bio*Shark is antiangiogenic or is effective in the treatment for cancer. There have been no specific studies of Bio*Shark evaluating its bioavailability, absorption, distribution, metabolism, excretion, pharmacokinetics, pharmacodynamics (antiangiogenic activity), or dose response. There are no good data on the amount of antiangiogenic activity/gram, milligram, microgram, or nanogram of crude shark cartilage or the shelf-life of that activity. The argument that hundreds of thousands of patients have been "treated" with shark cartilage or that the "proof lies in the pudding" does not answer the myriad of unknowns regarding shark cartilage or justify its use in cancer patients. Because the most effective dose or dose schedule has never been established, it is not possible to offer adequate directions for the use of Bio*Shark in cancer patients.

In summary, there is no competent and reliable scientific evidence that any crude shark cartilage product has any proven efficacy in treating human cancer. Furthermore, the supporting nonclinical studies of crude or partially-purified shark cartilage products are extremely limited, particularly with regard to mechanisms of action, pharmacokinetics, pharmacodynamics, establishment of the MTD and recommended Phase II/III dose, all essential components in clinical drug development.

b. 7 Herb Formula

The key questions relating to 7 Herb Formula are:

- Is 7 Herb Formula effective in the treatment or cure of cancer?
- Does 7 Herb Formula inhibit tumor formation?

Conclusion

A thorough review of peer-reviewed literature and all of the documents produced by DCO indicates that there is no reliable and competent scientific evidence that 7 Herb Formula is effective in the treatment or cure of cancer or that it inhibits tumor formation.

Discussion

7 Herb Formula contains Burdock root, sheep sorrel, slippery elm bark, Turkish rhubarb root (the 4 ingredients of another product called Essiac, which has never been evaluated in clinical trials to determine if it has any anticancer activity), cat's claw, Siberian ginseng, and watercress. Unlike the other DCO products under review in this report, the concentrations of the seven ingredients are not provided in the label. Thus, the amount of each ingredient in the DCO-recommended total daily dose of 2 to 4 ounces of 7 Herb Formula is unknown.

I will now review briefly published data about each of the components of 7 Herb Formula. Of note is that according to the label, an ounce of 7 Herb Formula contains no calories, carbohydrate, protein, or fat, and no cholesterol or sodium. The label also indicates that each ounce contains 2% of the daily value of vitamins A and C but no other vitamins, and no calcium or sodium. An analysis of the constituents of 7 Herb Formula is provided in Table 2 and suggests that the label is misleading and in error or both. If indeed 7 Herb Formula contains no carbohydrates, proteins, or fats it must be inert with respect to nutrients. My understanding is that most plants contain carbohydrates.

Table 2. Constituents of Components of 7 Herb Formula (from Cassileth and Lucarelli)

Constituent	Carbohydrates	Fats/cholesterol	Vitamins	Other ingredients
Burdock root	Inulin, mucilage, pectin, flavonols, polyphenols (quercetin), Phytosterols	Fatty acids, polyacetylenes, volatile oils,		Bitters, tannins
Cat's claw	Oxindole alkaloids, glycosides, polyphenols,			Tannins,

Sheep sorrel	Glycosides,		A, B complex, C, D, E, K	anthraquinones Oxalates, tannins
Siberian ginseng	Polysaccharides, glycosides, eleutherosides, glucose, maltose, sucrose,	Oleanolic acid, terpenoids, volatile oils, coniferyl aldehyde		Caffeic acid
Slippery elm bark	Mucilage, galactose, glucose, galacturonic acid,	Physterols; fatty acids (oleic, palmitic); cholesterol		Tannin, calcium Oxalate
Turkish rhubarb root	Starch	Fatty acids, volatile oils		Anthraquinones, tannins, calcium oxalate,
Watercress	Glycosides		A, C, E, nicotinamide	Nitriles, calcium, iodine, copper, manganese iron, phosphorus,

Neither nonclinical nor clinical studies of 7 Herb Formula have been reported in peer-reviewed literature. Thus, there is no evidence to support claims that 7 Herb Formula or any of its individual components are effective anticancer agents or inhibit tumor formation. Nonclinical and clinical studies of the individual components of 7 Herb Formula will now be reviewed.

Burdock root: Neither nonclinical nor clinical trials have been reported in cancer patients. In mice, burdock root stimulated macrophages (cells that phagocytose other cells, bacteria, and other debris). Other studies suggest that burdock root may induce hypoglycemia and increase carbohydrate tolerance. Other reports indicate that some Burdock root products were contaminated with belladonna alkaloids (atropine).

Cat's claw: An indole alkaloid from the tree *Uncaria tomentosa,* cat's claw appears to have immunostimulatory activity in vitro by enhancing phagocytosis and T-helper cell function, and inhibiting NF-κB and TNF-α, and increases myelopoiesis. Anti-inflammatory activity was also noted. (Sandoval et al, 2002) Cat's claw inhibits CYP3A4 and thus will increase the serum levels of a number of drugs including protease inhibitors,

non-nucleoside reverse transcriptase inhibitors (NNRTI) and cyclosporine. It increases the activity of antihypertensive agents causing hypotension, causes diarrhea, and has anticoagulant and antiplatet activity, increasing the risk of bleeding. In cancer patients with low platelet counts, this could be very dangerous. In vitro, cat's claw inhibited the growth of breast cancer cells (Riva L et al, 2001). To that extent tat cat's claw enhances DNA repair after chemotherapy, this might actually interfere with the chemotherapy by preventing programmed cell death of cancer cells.

Published results from clinical trials of cat's claw in cancer patients do not exist. Thus, there is no established or recognized role of cat's claw in treating human cancer or causing regression of tumors in cancer patients.

Sheep sorrel: Simply stated, there are no published clinical trials of sheep sorrel in cancer patients. Adverse side effects include low potassium levels in the blood. Thus, its efficacy as an anticancer agent has not been established.

Siberian ginseng: Siberian ginseng comes from the root of *Eleutherococcus senticus* and anecdotally is thought to be an enhancer of physical and intellectual performance and an immunostimulant. Most of the data supporting the mechanism of action and beneficial effects of Siberian ginseng not surprisingly came from Russia. Some of the constituents of Siberian ginseng bind to estrogen, progestin, and mineralocorticoid and glucocorticoid receptors, which might have an effect on cell proliferation. Stimulation of T-lymphocytes and natural killer cells has been reported but the mechanism of this immunostimulation is unknown. (Cassileth and Lucarelli, 2003) Randomized, controlled clinical trials in cancer patients have not been reported.