DIETARY SUPPLEMENTS AND THE DSHEA OF 1994-

IS REFORM NEEDED TO ENSURE SAFETY?

By

MATTHEW T. RYCYK

(Under the Direction of GARY DYKSTRA)

ABSTRACT

The Dietary Supplement Health and Education Act of 1994 provides for a much different set of regulations than those that cover pharmaceuticals and conventional food products. Under this law, the dietary supplement manufacturers are responsible for ensuring that the supplement is safe before it is marketed. However, no efficacy claims can be made because clinical trials are not required. Manufacturers do not register their products and do not have to receive approval before marketing. It is the responsibility of the FDA to monitor safety in the post-market environment.

In the years since the passing of the DSHEA, there have been instances where supplements have not been safe for use. Through a critical change analysis of the issues and gathered expert opinions this research addresses two questions: Are dietary supplements safe for use or is there need for reformed DSHEA legislation to ensure safety?

INDEX WORDS: DSHEA, FDA, HERBAL SUPPLEMENT, cGMP, DIETARY SUPPLEMENT

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DEDICATION

I would like to dedicate this work to my godfather Robert “Bubba” Sullivan who through his passing gave me the opportunity to pursue this degree. You are always in our hearts big guy. You are truly missed. Also to my beautiful wife Jennifer who sat through weekends alone while I was on the computer doing school work. Your patience for this process has made us that much stronger. My grandmother Celeste Rycyk was also an influence to me during my life, she will be missed.

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Chapter 1

Introduction

The passage of the Dietary Supplement Health and Education Act of 1994 **(**DSHEA**)** has allowed many companies and individuals to make millions of dollars on dietary supplements which do not have to be proven efficacious. There have been many instances since 1994 where consumers have experienced adverse events when taking dietary supplements. These adverse events have been caused by adulteration, contamination, and improper dosing to name a few. The purpose of this research was to evaluate changing the DSHEA legislation from a critical change perspective to ensure these products are safe. The research will be focused on changes to funding, public adverse events information, the creation of a GRAS (generally recognized as safe) list, and product registration and user fees. This research builds extensively off of the works of Dan Hurley and Dr. Stephen Barrett, both of whom are reputable advocates for changes to DSHEA. Upon completion of this research, more extensive studies will be apparent and could be completed in the areas of funding and adverse events which should be more quantitative rather than qualitative. The suggestions made in the conclusions of this research will give a regulatory perspective of what needs to be done through legislation and other routes to ensure the safety of the dietary supplements.

The History of Dietary Supplements

Homeopathic medicine came about in the late 19th century. Many physicians looking for an alternative approach to modern medicine turned their efforts to non-conventional therapies in

order to treat disease states. "A successful lobbying effort at the state level for licensure of medical schools and doctors under an allopathic system was brought fourth." (27) The 1938 Federal Food, Drug, and Cosmetic Act had very little information with respect to vitamins and alternative therapies, because most vitamins were not discovered until the late 1920 and the true benefits until even later on. Even though the benefits of vitamins and supplements were not well established, the homeopathic and allopathic thoughts on modern medicine continued to develop therapies over the next 50 years in the United States. (27)

In the 1960s the FDA published a proposal on maximum and minimum nutrient limits, recommended daily allowances (RDAs). (27) An opposition began to emerge as the public began to feel that the FDA was encroaching upon their rights to determine how they wanted to supplement their diet. (27) Over the next 15 years, a number of attempts were made to put maximum limits on potency with regards to vitamins and supplements. In 1973, the FDA issued its final ruling restricting vitamins and minerals to 150% of the RDA value, any product in excess of this limit would be deemed a drug. (27) This was overturned yet again in 1976 by a bill which became section 411 of the Federal Food Drug and Cosmetic Act. (27) The Nutrition Labeling and Education Act (NLEA) was passed in 1990. The FDA commissioner at that time, Dr. David Kessler, wanted to use this act as a way to reestablish the FDA's hold on the dietary supplement industry. The act gave the FDA the authority to approve disease prevention claims for all food products. (28) Dr. Kessler stated that the FDA would not approve any disease prevention claims for dietary supplements, even if they were approved for foods. (28) Dr. Kessler then commissioned a "Dietary Supplements Task Force" headed by Gary Dykstra to create a scientific report on the complex and controversial topic of dietary supplement regulations. (32)

A ninety-three page report was created by the Task Force together with industry. The "Dykstra Report" as it came to be known, grouped dietary supplements into three distinct categories. The following bullets are the categories with additional recommendations provided directly from the final report:

1. Vitamins and Minerals- The task force determined that for some vitamin and mineral supplement products, safety was not a concern. However, most essential nutrients are toxic when consumed in excess, and FDA-established safety level provide a benchmark for avoiding potential hazards in such cases. (31)
2. Amino Acids- The task force expressed a serious concern about the safety hazard from high potency amino acid products. They are marketed and purchased for uses that essentially make the products drugs. The task force thus recommended that the FDA initiate rulemaking to categorize each of the individual amino acids as drugs when sold in a capsule or tablet form. The only exception would be for products in which the amino acid is present at a level demonstrated to be safe and have a recognized food/nutrient function. (31)
3. All other Dietary Supplement Products- The task force recommended the continuation of the food additive provisions of the statute unless drug claims were made about the supplement. The FDA maintained the stance that their principle interest was to ensure that these products and their ingredients are safe. Working with industry, the FDA would also need to update the generally recognized as safe list and provide the scientific determination of how products could be placed on that list in the future. (31)
4. Additional Recommendations:- The additional recommendations the task force made focused on the need to establish good manufacturing practices, purity and identity

> standards, and disintegration and dissolution standards to ensure bioavailability. They stressed that purity standards are an integral party of ensuring safety. In addition, it would help ensure that consumers are getting what they pay for. (31)

The conclusions of the task force state "The task force believes that its recommendations should recognize a role for dietary supplements in ensuring a balanced diet and, with safety as an underlying principle, freedom of choice for these products should be allowed as much as possible."(31)

The report was presented to the FDA by the task force in early 1991. (32) Dr. Kesseler then handed off the report to another high ranking official at the FDA. The agency did something which caused industry to finally take action to push forward with DSHEA. They did not use the suggestions stated by the dietary supplements task force in the report for another year. The report was finally listed in the Federal Register in May of 1992. By this time, industry had already initiated the ground work for what would become the DSHEA. Industry was concerned that with passing time the FDA would to regulate all supplements as drugs. There was distrust in the dietary supplement industry of what the FDA was doing or planning with the passing time. Even after the report was published, nothing was being done to change the regulations accordingly. (32) The industry became afraid of what the FDA was preparing so it was in their best interest to act first. Industry did act by developing and quickly passing DSHEA in 1994. The FDA was surprised when DSHEA passed through legislation. The DSHEA is still controversial today.

A grassroots movement of consumers and industry personnel began to develop around the time Dr. Kessler stated no more health claims would be approve for dietary supplements. This movement has been widely regarded as one of the most successful political movements in

the history of America. (28) A group of consumers who were adamant about keeping their supplements in their diets and out of government control. They did not believe in the pharmaceutical industry. They had distrust of pharmaceuticals and the drug development process. (24) The FDA was perceived as a "corrupt" organization which flexed its muscles in places where they did not belong. (24) This group coveted their right to consume supplements as much as the rest of America covets the right to vote. They wanted a homeopathic alternative to modern medicine.

Dietary supplement advocacy groups began to develop as a result of increased regulation by the FDA. The Natural Products Association was established in 1936. (29) The Council for Responsible Nutrition established in 1973 was one of the first purely for dietary supplements. (3) The United Natural Products Alliance was formed in 1991. These groups were advocates for industry and consumers' rights during the passage of DSHEA.

Battling the grassroots movement was a large number of people who believe it is the sole purpose of the dietary supplement industry is to mislead the consumer. This opposition group is based upon the complete lack of scientific evidence that support dietary supplement structure-function claims. There is no requirement for premarket approval of a dietary supplement in the United States. Therefore, proof of efficacy does not have to be established for dietary supplements. There is a belief that these products do nothing beneficial and are marketed by manufacturers looking to make a quick buck on the naive consumer. (25)

Over the past years there have been numerous accounts of tainted dietary supplements causing severe health problems. Many are outlined in Dan Hurley's book "Natural Causes: Death, Lies, and Politics in America's Vitamin and Herbal Supplement Industry." In Mr. Hurley's book, he outlines some of the most severe cases of health problems ranging from

kidney failure and cancer caused by aristolochic acid tainted products to thousands of cancer patients believing shark cartilage was going to cure them of cancer. He gives clear examples where false information from industry resulted in the deaths of real people.

The number of people aware of the need for increased dietary supplement regulation increased as a result of the misleading of the consumer that went on during the Ephedra ban. (30) The Ephedra ban was critical in making the divide between the two groups even more apparent. (30) Advocacy groups such as Public Citizen came to the forefront against dietary supplements and were essential in seeing the ban of Ephedra all the way through. (25) Ephedra is one of the only dietary ingredients to have been successfully removed from the United States market under DSHEA regulations. Still to this day the anti-supplement movement remains resolute in their efforts to have additional products removed from the market.

Chapter 2

Background Research

Federal regulation governing products regulated by the FDA change every year. Significant changes in how dietary supplements have been regulated in the United States were created with the passing of the Dietary Supplement Health and Education Act of 1994. The DSHEA required the manufacturer to assure the dietary ingredient/supplement is safe before marketing. It also created the definition of a dietary ingredient/supplement. (1) The FDA is responsible for taking action against unsafe dietary supplements once the product is on the market. (1) There is no pre-market approval process for dietary supplements analogous to the review process for pharmaceuticals or medical devices. In addition, the post-marketing responsibilities of the FDA include monitoring of safety, adverse events, and product information.(1) The lack of review process coupled with the overwhelming post-marketing responsibilities that the FDA must endure as a result of DSHEA has resulted in questionable products reaching the market.

Since the passing of the DSHEA, there has been an increase in the number of dietary supplements reaching the market that are later deemed by the FDA to be adulterated, misbranded, or outright unsafe for use by the public. This is supported by the numerous recalls that have been issued by the FDA. (1) Adverse events have been required to be reported since January 1, 2008. In the first six months of reporting, there were 604 adverse event reports. (2) Industry organizations and the FDA claim many of the adverse events that are reported are due to underlying medical conditions that existed before the consumer started taking the product. (2)

The paradox is that there is no way to disprove this argument because the true side effects of dietary supplements are not disclosed in the labeling through proper clinical trials. There were 600+ adverse events from dietary supplements compared to the over 250,000+ for the same time length for prescription and OTC products. (2) The number of adverse events reported from dietary supplements dwarfs adverse events pharmaceuticals. (2)

There is an ongoing battle between advocacy groups for industry, consumers, and government on what should be done. Industry wants to self-regulate and keep the laws the way they are currently written. Any increase in government oversight would be a threat to the more than 20 billion dollar a year revenue of the industry. (3) The supplement industry states that the FDA has adequate authority to remove unsafe products from the market and protect public health. (3) Stephen Barrett, M.D., a retired psychiatrist who resides near Chapel Hill, North Carolina, has achieved national recognition as an author, editor, and consumer advocate. (3) In addition to heading Quackwatch, he is vice-president of the National Council Against Health Fraud, a scientific advisor to the American Council on Science and Health, and a Fellow of the Committee for the Scientific Investigation of Claims of the Paranormal (CSICOP). (3) Dr. Barrett states on his website, quackwatch.org that "Congress has only given the FDA the authority to act after substantial harm has already occurred." (4) "How is the FDA going to know what products have harmful substances and who has been taking them?"(4) Many government officials are split on this issue. People enjoy their right to supplement their diet and at the same time want safe products on the shelves in the store. The fact still remains that many consumers are still not well informed when it comes to decisions about taking dietary supplements.

This work hopes to develop the issues brought forth in the works of individuals like Dr. Stephen Barrett and advocacy groups such as Public Citizen into recommendations for changes to DSHEA while considering industry input and impact as well. A fair and balanced perspective of the available information and collected research from individuals on both sides of this issue will create a picture of the critical issues facing the dietary supplement industry. The findings of this research should contribute to the understanding of what needs to be done in the future to ensure the public is safe, and more aware of the supplements they consume. In a recent speech, Dr. Margaret Hamburg, Commisioner of FDA, she stated that in the past the FDA has been slow to act on issues concerning public safety. She specifically stated that: "The agency will no longer issue multiple warning letters to non-compliant firms before taking enforcment action. We will now consider immediate action to egregious violations and consider immediate action even before we have issued a formal warning letter."(5) This research paper will present facts and perspectives from both sides and through constant comparision analysis suggest changes to DSHEA as well as general improvements that can be made to better regulate the safety of dietary supplements in the United States.

Development of the Act

The Dietary Supplement Health and Education Act of 1994 was enacted by Congress following public debate concerning the importance of dietary supplements in the promoting of health. (10) Congress had determined that "improving the health status of the United States' citizens ranked at the top of national priorities of the Federal government." (10) The people of the United States needed access to current and accurate information about dietary supplements and clarity of the FDA's regulatory approach to these products. (10)

Prior to DSEHA, in 1990 the Nutrition Labeling and Education Act was passed and signed by President George Bush. (12) This legislation was to improve the information regarding health claims made about dietary supplements. (12) According to industry, the wording of the law gave the FDA a broad scope of what they could regulate. (12) There was an overwhelming feeling that the agency was over-regulating dietary supplements and safe and beneficial nutritional products were being unfairly scrutinized. (12)

The FDA went on the offensive in 1991. "The FDA began using the food additives provisions of the law to go after dietary supplements the FDA did not like." (12,24) The then acting commissioner of the FDA, Dr. David Kessler, commissioned a panel to create a report on what the FDA should do if they were to start fresh with dietary supplement regulation. (12) A result of this report was the Health Freedom Act was introduced by Senator Orrin Hatch to protect the rights of the public to have a choice for safe and effective dietary supplements. (12) This act was the basis of the DSHEA though the Health Freedom Act was never passed. (12)

A grassroots movement, started by industry advocacy groups, developed and mobilized the public against the FDA. A raid against a clinic in Tacoma, Washington created even more interest in the movement. (12) Dr. Jonathan Wright, a physician in Washington State was prescribing L-tryptophan. (12) The FDA had issued a temporary ban on the product as a dietary supplement. (12) However, use of L-tryptophan had not been banned for use for medical purposes; Dr. Wright continued to prescribe L-tryptophan to his patients. In August of 1991, the FDA seized all of his L-tryptophan. Subsequently, Dr. Wright filed suit against the FDA. (13) On May 6th, 1992 the FDA raided Dr. Wright's clinic with armed sheriff's officers who seized vitamins, records, and questioned his patients. (12) It was later found that the raid was

retaliation for the lawsuit which was filed against the FDA. The raid became known as the "Great Vitamin B Raid". (13)

A result of the raid was a very well-known public service announcement which starred Mel Gibson. (12) In the video, federal service agents in Special Forces gear raid a house where Mel Gibson is living. (12) He holds up a dietary supplement bottle and says "Guys, Guys, It's only vitamins." (12) As Gibson's character is being taken away in handcuffs he says "Vitamin C, you know like in oranges?" (12) The video, though very dramatic, was not far off base of what was really happening to supplement retailers and clinics at the time. (12)

A vote was forthcoming in the house and senate on regulatory reform of dietary supplements in 1994. Industry professionals such as Jarrow Rogovin of Jarrow's Formulas, attorney Scott Bass, and attorney Loren Israelsen devoted time and resources to the battle against further regulation of dietary supplements as drugs. An interesting fact is that these same individuals were working with and giving input to the FDA dietary supplement task force just two years prior. (32) The Democrats were in control of the house at the time and were in danger of losing a large number of seats in the upcoming elections. (12) Senators Hatch, Kennedy, Harkin, and Waxman and Congressman Dingell were able to develop a bill known as the Dietary Supplement Health and Education Act was created. (12) "It was written in a specific manner to keep dietary supplements within the framework of the current food law and statutory interpretation."(12) The FDA never expected the bill to pass through congress. (12) A result of the passing of DSEHA, the supplement industry grew from a 4 to a 12 billion dollar a year business within a year. The current numbers stand around 25 billion dollars a year in sales of dietary supplements and continue to grow every year. (33)

FDA Framework DSHEA

The term “dietary supplement” in the DSHEA Act of 1994 is defined as a product taken by the mouth that contains a “dietary ingredient” intended to supplement the diet. (1) The term “dietary ingredient” in the supplement can be one or a combination of the following: vitamin, mineral, herb, botanical, amino acid, enzyme, organ tissues, glandular, metabolite. Dietary supplements can be sold in many forms such as concentrates, tablets, capsules, softgels, powders, liquids, or bars. (1) The form the supplement is presented is not important, rather the product must not be represented as a conventional food product and must be labeled accordingly.

The DSHEA Act also defined the terms “new dietary ingredient” and “dietary ingredient” as related to the components of dietary supplements. An ingredient of a supplement must be a vitamin, mineral, herb, botanical, amino acid, supplement to the diet that increases dietary intake, concentrate, metabolite, constituent, or extract. (1) They can be used alone or be a combination of two of these. A ‘new dietary ingredient” meets one of these requirements for the definition of “dietary ingredient” and was not sold in the United States in a dietary supplement before October 15, 1994. (1)

Contrary to public belief, DSHEA places the responsibility of determining the safety of a dietary supplement on the manufacturer prior to marketing. The interesting fact concerning safety is that DSHEA establishes separate standards for the safety of dietary supplements by describing the conditions under which they are considered adulterated. The act defines the regulatory requirements for labeling as well. (1) Any representations or claims made by the firm marketing a product must be supported by sufficient evidence. (1) The act also clearly states that dietary supplements do not need approval from the FDA prior to marketing. (1) A firm does not have to register the product, or itself, before producing and selling a dietary supplement. (1) The

only instance in which a firm must notify the FDA is when the dietary supplement contains a "new dietary ingredient". (1) Then, and only then, does the manufacturer have to demonstrate to the FDA why the ingredient is expected to be reasonably safe for the general public to consume. (1) There is no generally recognized list of dietary ingredients on the market before October 15, 1994. (1) It is the responsibility of the manufacturer to determine if the dietary supplement was marketed before October 15th, 1994 and to provide the documentation to the FDA if needed.

Under DSHEA, all ingredients must be clearly marked on the label of a dietary supplement. (1) Labeling must be specific with information including a descriptive name of the product stating that it is a "supplement", the name and address of the manufacturer/packager/or distributor, ingredients, and net contents. (1) A standardized supplement facts panel should list the ingredients one by one. (1) The other ingredients used but not deemed suitable for the supplement facts panel (other food stuffs, processing aids, allergy information) should be listed below the facts panel. (1) Dosing requirements fall upon the manufacturer to ensure safety. There are no rules to limit a serving size or the daily amount of the nutrient in any form, and does not require FDA approval. (1)

Label Claims and Promotion of Dietary Supplements

According to Section 5 of DSHEA, any information about a dietary supplement that is published such as an article, book chapter, peer abstract, or leaflet which is reprinted in its entirety is not considered to be labeling. These publications may be used in the sale of the product provided that they are truthful and not misleading. These publications also must not promote a particular brand of dietary supplement and present a balanced view of the scientific information. (10) These publications are not reviewed by the FDA in anyway except in the

instance of a complaint. The vast amount of promotional material for dietary supplements from various media sources makes effective regulation virtually impossible. When third-party publications are used, they must also be kept physically separated from the product in the storefront as required by DSHEA. (10) Traditionally, the FDA has considered literature used directly in connection with the sale of a product as labeling as in the case with pharmaceuticals or medical devices. (15)

The FDA allows three different types of claims to be made in dietary supplement labels. They are health claims, structure/function claims, and nutrient claims. (6) It is the responsibility of the manufacturer to ensure the claims are valid. (6) "Prior to the passage of DSHEA, a dietary supplement for which a health related claim was made was regulated either as a drug, which had been shown to be safe and effective before marketing, or as a food, for which prior authorization to make a health claim was required if the claim concerned a disease or health related condition." (9) Under DSHEA, the dietary supplement claim does not have to be proven in a clinical trial as pharmaceutical drugs do. The FDA can question the manufacturer if they believe false claims are being made. If the manufacturer is improperly advertising the product, it falls under the jurisdiction of the Federal Trade Commission and not the FDA. (6)

Health claims are the most widely used promotional claim by the supplement industry. Health claims describe a relationship between a food, food component, or dietary supplement ingredient and reducing the risk of a disease or health related condition. (6) The FDA has published a food labeling guide to allow for a list of generally used health claims based upon scientific evidence compiled over many years. The health claims undergo extensive scientific review and are usually the result of a health claim petition and establish the nutrient/disease relationship using science as a base of evidence and are known as the NLEA health claims. (6) In

all cases, the claim must be followed by the statement "This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease." (8)

Structure/function claims are also widely used in the supplement industry. With the passing of the DSHEA, some new regulatory procedures for structure function claims on dietary supplements were established. Structure/function claims take the role of a nutrient/dietary supplement in the body, and describe how it has an effect on the structure of the human body. The claim may also establish how the nutrient/dietary supplement acts to maintain the structure or function of the body. It is the manufacturer's responsibility to make sure these claims are truthful; they should not be misleading to the consumer. The claims are not pre-approved by the FDA prior to marketing; however notification should be made to the FDA 30 days after marketing if the structure/function claim is made on the label of a dietary supplement. (6)

The final type of claims associated with dietary supplements is nutrient content claims. As with foods, dietary supplements can be described by the level or nutrient content of the product. Key words such as low, free, and high are used to describe the content. (6) These claims also compare the content of the supplement against the content of another product. "Most nutrient claims regulations apply only to those nutrients or dietary substances that have an established daily value." These types of claims are used frequently and are meaningful to consumers. The FDA has outlined the rules for nutrient content claims in Chapter 6 of the Food Labeling Guide. (6)

New Rules of 2002

The FDA proposed new rules about structure function claims of dietary supplements as they relate to effects on the body in April of 1998. The new rules included the following: (16)

- Disease claims are not permitted
- Disease is defined as “any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof of the body that is manifested by a characteristic set of one or more signs of symptoms.”
- “Signs or symptoms” include laboratory or clinical assessments that are characteristic of a disease, such as an elevated cholesterol fraction, uric acid, or blood sugar, and characteristic signs of disease, such as elevated blood pressure.
- A claim that a product helps protect against a disease
- A product name that implies an effect on a disease, the name must be generic and non-descript
- Suggestions that a product helps fight a specific disease or type of disease by stimulating the body’s defenses would be a disease claim, but general claims such as “supports the immune system” would not be a claim. (16)

An enormous amount of support from the supplement industry and its advocates caused the FDA to revise its final rule on health claims for dietary supplements. The FDA received over 100,000 protest messages concerning the proposed rule. (15) The supplement industry did win a minor victory allowing health-maintenance claims such as “for muscle enhancement” or “supports a healthy immune system”. (15) However, direct and implied disease claims are no longer allowed as a result of this regulation. Some conditions such as osteoporosis or other serious conditions associated with aging, menopause, or adolescence will still be treated as diseases. (15) Industry was not happy with the legislation because it restricted their promotion of dietary supplements. The final rule published in 2000 and made effective in 2002, to remove

erroneous claims that many dietary supplement manufacturers were using to sell their products. It made the claims much more general to lay persons to understand and prevented direct correlation to a disease state.

Case Study of Ephedra

Ephedra came on to the dietary supplement market in early 90's as a metabolism booster, performance enhancer, and weight loss product. The Chinese had been ingesting the herb, Ma Huang (Ephedra sinica), for almost 3,000 years as a stimulant. (17) The herb is known to constrict blood vessels and increase blood pressure and heart rate. It also has a thermogenic component which causes an increase in metabolic rate. (17)

The supplement industry was selling millions of dollars worth of Ephedra each year. The usage of Ephedra by athletes became widespread. (19) People were using the product for increased energy and performance on the field, in the gym, or on the track. Adverse events started to be seen as wide spread. Many of these products were being taken in instances where the body was already being stressed to its maximum potential. People were unknowingly taking multiple products which contained Ephedra. Escalating the problem further, major discrepancies between the amount of Ephedra on the label of product and the amount contained in the product. (18) There was absolutely no content uniformity with variations of 10-fold seen within one lot of product. (18)

A number of prominent athletes died in the years following the Ephedra hype. The deaths of Steve Belcher of the Baltimore Oriels, Korey Stringer of the Minnesota Vikings, and Rashdi Wheeler of Northwestern University have been linked to the consumption of Ephedra prior to their deaths. While there was no definitive way to determine if the Ephedra caused the

deaths of these men, it was found in their systems post-mortem. In 2002, the Department of Justice forced the company Metabolife to turn over reports of adverse events associated with Ephedra. There were over 15,000 of these reports. (19) Considering how much of this product was sold compared to the adverse events is a difficult task. However, from the number of adverse event reports generated there seemed to be a connection between the use of Ephedra and adverse events. The FDA stepped into action and issued a press release on December 30th, 2003 recommending that consumers stop buying and using Ephedra. (1) On the 12th of April 2004 there was a final ruling banning the use of all Ephedra containing products. Metabolife had created an environment of distrust by withholding evidence of issues associated with Ephedra. A feeling of mistrust lasts till this day with some of the hard line DSHEA reformists.

The dietary supplement industry fought back hard. The FDA had just banned one of its most successful and effective products. The Nutraceutical Corporation decided to challenge the FDA's ban. The basis of the claim was that the FDA had failed to prove that low doses of Ephedra were unsafe. As a result, the ban was lifted in the State of Utah and enforcement in the rest of the country became unclear. (22) The case was appealed to the Tenth Circuit US court of Appeals in Denver, Colorado and on August 17th, 2006 the ban was upheld. After millions of dollars of tax payers' money being spent on hearings and court proceedings the American public is now safe from Ephedra. Dietary supplements containing Ephedra remains illegal in the United States. (23) To this date, Ephedra is the only dietary ingredient to be successfully removed from the market under DSHEA.

Additional changes of 2006

In December of 2006, significant changes were enacted by Congress concerning dietary supplements and their manufacture. The Dietary Supplement and Nonprescription Drug Consumer Protection Act (S. 3546) was passed requiring manufacturers to now report and notify the FDA about serious adverse events related to their products. "At the start of December 2007 manufacturers must report deaths, life-threatening experiences, inpatient hospitalizations, persistent or significant disability or incapacity, birth defects, or the need for medical intervention to prevent such a problem." The bill also requires manufacturers to now place a telephone number or address on the product labels so consumers can contact them in the case of such an event. (15)

These improvements were a direct result of the Ephedra ban which had taken place due to the number of adverse events. (15) There was a public outcry from many lobbyist groups in Washington, D.C. to have something done to prevent harmful products from entering the market. As far as many of the groups were concerned, dietary supplements should cause no adverse events whatsoever or risk being removed from the market. Industry had issues with the reporting of adverse events because of many contributing factors. Many individuals are on prescription medications in addition to their supplements making it difficult to determine if the cause was from the supplement or the medicine. Many people also take a number of supplements rather than just one making it difficult to determine which supplement caused the adverse event. Consumers also do not realize that the supplement may be the cause of the problem and just fail to report the event all together.

Current Good Manufacturing Practices

In June of 2007, after much debate, the FDA finally published the final rule for Current Good Manufacturing Practices for Dietary Supplements. The rule became effective on August 24th, 2007, but was written to allow companies a 36-month window of time to comply depending on the size of the corporation. (20) Public comment on this topic had been extended for almost two years because of many issues the supplement industry had concerning the topic. The ruling applied to companies that manufacture, package, or store dietary supplements however retailers were not included in the ruling and health care practitioners were to be considered on a case-by-case basis. (20) Dr. Robert Brackett, the director of the Center of Food Science and Applied Nutrition, was quoted as saying that the "final rule will help ensure that dietary supplements are manufactured with controls that result in a consistent product free of contamination, with accurate labeling." (20) This has been the goal of the FDA for a number of years and with the passing of the Current Good Manufacturing Practices (cGMP) ruling the agency seems one step closer to safer more consistent supplements.

The 800 page cGMP document directs supplement manufacturers on how to test their products for identity, strength, purity, and composition. The hope is that the finished products contain actual contents labeled on the products. Concerns over adulterants have been an issue for years and now the FDA has a way to consider these products adulterated or misbranded. The ruling also contains very specific instructions on quality control, constructing of manufacturing plants, finished product testing, complaint and record keeping, and establishment of standard operating procedures. (20).

The ruling mandates one hundred percent testing on ingredients used in the dietary supplements produced. The United States Pharmacopeia is working on testing monographs for

many of the currently used ingredients in dietary supplements. The FDA has outlined specific instructions on exemptions for testing of products which have not yet been fully established. (20)

While many industry advocates see the cGMP ruling very hurtful to the small manufacturer, they also recognize the need for cGMPs to establish a better sense of trust with consumers.

Chapter 3

Methodology

The purpose of this research is to evaluate the perspectives of prominent professionals from industry, regulatory bodies, and safety advocacy to assess the impact of DSHEA, changes to funding, public adverse events information, the creation of a GRAS (generally recognized as safe) list, and product registration and user fees. Qualitative data was collected through one-on-one interviews and analyzed using a constant comparison process. The integration of conceptual data reveals patterns and consensus among a group of vested individuals regarding the regulation of dietary supplements. Data analysis provides specific recommendations for the enhanced safety and use of these supplements.

The qualitative perspective used for this research is based upon a particular social scientific perspective known as "critical theory". This segment of philosophy is based upon the works of Western European Marxist theorists who were known as the Frankfort School. (35) Critical theory is oriented toward critiquing and changing society as a whole, in contrast to traditional theory oriented to understanding or explaining it. (35) This theoretical perspective takes writer's concepts of societal change on an issue for the betterment of society as a whole. Critical theory includes self reflection of the researcher, who typically has personal interests and opinions regarding the topic. These perspectives are therefore disclosed as part of the interpretation of the societal issue being studied and where there is a vested interest of many people, in this case, dealing with the issue dietary supplement safety. This work will interpret perspectives of key individuals who hold unique viewpoints regarding current dietary

supplement regulations, criticisms, means to amend them, and achievable practical goals for the transformation of the industry. (35)

In order to fully understand "a critical theory" perspective, a detailed explanation of the writer's background and thoughts on the subject before the start of the research should be provided. Typically an outside interviewer should conduct an interview of the writer prior to beginning of the research. In the case of this research, an outsider was not used. However, in order to provide the necessary background information, the following paragraph will be a brief synopsis of the writer of this research and his perspective of DSHEA.

"My name is Matthew Rycyk and I am a graduate student in the University of Georgia's pharmaceutical and biomedical regulatory affairs program. I am currently employed in the pharmaceutical industry as a chemistry manufacturing controls regulatory associate. My undergraduate degree is from the University of Illinois is in Animal Sciences. I have worked in the academia and industry for the past eight years conducting medical research, pre-clinical research, and regulatory affairs. I am also regulatory affairs certified in the United States. My perspective is unique in that through my studies I have come to know and understand why regulations are in place. It is essential that industry and their regulatory agencies have a mutual respect for each others' position. I am also a dietary supplement consumer. My perspective at the beginning of this research is that the dietary supplement industry lacks the adequate regulations to provide safe products to consumers. An improved system of checks and balances must be created in order to ensure safety goals are met. An overhaul of the DSHEA regulations is the first place which reform needs to take place. I do not believe in the safety of some dietary supplements on the market today, though I do believe there are some companies currently trying to do right by the consumer."

In researching DSHEA there were two apparent schools of thought on dietary supplements. Those who support the DSHEA and those who would like to see changes take place. As with most social movements, there are factions or cliques. (47) In order to fully understand the issue as a whole, each faction should be evaluated. Interviews were conducted with people associated with the passing of the DSEHA Act as well as advocates for public safety from dietary supplements. The process for choosing the participants in this research was fairly straight forward. I questioned Gary Dykstra my thesis advisor to advise me on whom I should contact in addition to doing web based searches to find the research participants. I identified people who were closely associated to industry (Scott Bass, Loren Isrealsen), regulatory bodies (Bill Frankos, Richard Cleland), advocacy groups (Peter Lurie), and a writer (Rebecca Wright). I analyzed their backgrounds and determined how they were associated with dietary supplement regulation in the United States. Once it was determined that each met the criteria of having significant expertise of five or more years with supplement regulation issues and or employment in the dietary supplement industry, twelve people were identified and contacted. Six of the twelve consented to be part of the research study. Attempts to contact other advocacy persons such as Dr. Stephen Barrett of Quackwatch.org and author Dan Hurley went unanswered. Additionally, a number of dietary supplement manufacturers were contacted such as Natrol, CytoSport, and Premier Research Labs. This additional information from these interviews would have strengthened this research. I was unable to obtain these interviews or receive consent to interview. The interviews give a representation of both sides of dietary supplement reform and the participants were recognized as experts in their respective fields. A research protocol was written, submitted, and subsequently approved by the UGA Office of Human Research Subjects Institutional Review Board (IRB) prior to starting any interviews with the selected experts.

Questions were proposed to help establish a public opinion on both sides of the issue for more or less reform. The researcher used a semi-structured interviews style that allows some flexibility in the interview questions. In semi-structured interviewing, it is not only the information but also the themes and categories of analysis that are generated from the responses of diverse movement participants. (47) The open-ended nature of this interviewing strategy makes it possible for respondents to generate, challenge, clarify, elaborate, or recontextualize understandings of social movements based upon earlier interviews. In addition, semi-structured interviewing makes it possible to scrutinize the semantic context or connotation of statements made by the participants. (47) In regards to this research, this scrutinization of the interview's context will be important to the analysis of the data.

The questions were developed based upon the stance of the person being interviewed. Questions were refined to fit the individual to avoid presenting a question where the answer was obvious. In some instances, I was only allowed thirty minutes with the individual. Therefore, the development approach of the question for each individual had to be tailored. The approach was to let each side speak about key issues and then propose new ideas for reform that would benefit the public knowledge with minimal impact on the industry. Much of the data collected was outside of the range of questions asked once the interviewees started speaking and therefore consistency between the questions and data collected does not always coincide. All data was recorded in written form and information used was uncensored. All persons interviewed consented to being interviewed and approved the data used prior to publication.

A constant comparison method was used for data analysis. The data relevant to the changes to dietary supplement regulations identified by the author were analyzed. Each item of data will be compared to the rest of the data and placed in establish the conclusion categories.

The phrases will be scored using a numeric scale by the author of this research. The process will create numeric data from the qualitative word data collected in the research interview process. A more detailed explanation of the constant comparison method used in this research is located at the beginning of Chapter 5.

Chapter 4

Research Data

To determine how the DSHEA was enacted and the thoughts behind how dietary supplements are regulated in the United States a request was sent to Scott Bass and Loren Isrealsen, the two lead attorneys who wrote the Act. Both agreed to a phone interview and the following excerpts on their thoughts on the Act and the future of the dietary supplement industry are provided.

Loren Isrealsen

Mr. Loren Isrealsen, J.D. is the executive director of the United Natural Products Alliance, a trade association for dietary supplement companies. He has been in the dietary supplement industry since 1982 and worked on regulations and commercialization issues. He was one of two lead attorneys working for the supplement industry during the passage of the DSHEA and with Scott Bass, wrote the complete DSHEA Act of 1994. I spoke to Mr. Isrealsen via telephone on October 13, 2009 and Mr. Bass on October 16, 2009. (24, 26) In the following paragraph Mr. Isrealsen explains how the DSHEA was brought forward.

> "There exists in this country a large number of individuals who do not wish to be part of organized medicine; they believe in less government involvement in their health choices. If they could opt out of the entire system they would, they have very little trust in modern medicine and the pharmaceutical industry. Dating back to the 1950s, there have been confrontations between the

FDA and the ancestors of the supplement industry. There always needed to be a clear understanding of the category of regulatory areas dietary supplements fell under. There was concern following the passage of the Nutrition and Education Labeling Act of 1990. There was a new middle ground where health claims on food products became subject to new regulatory review. It became quite clear through raids of naturalist doctors' offices and health food stores that dietary supplements were next on the FDA list to undergo reform. A grassroots effort of a number of well known supporters of dietary supplements started in Utah by me and a few others. Senator Orrin Hatch came on board as a supporter as did Senator Tom Harkin and Congressman Bill Richardson. Commissioner Kessler came into office and created a committee to create a report on how dietary supplements would be regulated if there was a "clean slate". This committee created the "Dykstra Report" which basically stated in parts that dietary supplements should be regulated like drugs and no structure function claims could be made concerning the products. Industry sprang into action and the Dietary Supplements Health and Education Act was created by me, Scott Bass, a few others. This Act allowed dietary supplements to be regulated as food products. The word choices particularly in section 201 of the act were very expansive to allow for future products which were unseen at the time. The goal was to stop the definition of a dietary supplement from moving around." (24)

Scott Bass

Since the passage of DSHEA, there have been few changes to the Act. One major change was FDA's promulgation of cGMPs for the dietary supplement industry which after many years of being spoken about are now reality. Attorney Scott Bass is currently a partner at Sidley Austin, LLP in Washington, D.C. who helped draft DSHEA and who works regularly with the dietary supplement industry. I spoke with Mr. Scott Bass concerning the passage of cGMPs and he had the following to add:

> "There is an extensive review process for safety of dietary supplements, but many manufacturers throughout the years have failed to notify the FDA when placing a new supplement on the market. To this day, there is no FDA list of supplements grandfathered in before October of 1994 which makes this process difficult to enforce. During the 1990s, there were funds that were earmarked for better oversight of the dietary supplement industry, but the money was not sufficient. When dealing with dietary supplements, potency and stability count for quality products. The government held back on the issuance of cGMPs for the dietary supplement industry because they wanted to see the industry implode on itself, hoping consumers would loose confidence in the products before they stepped in to help. I believe the cGMPs will help the industry but they fail to place any responsibility on suppliers, and places the quality burden on the final manufacturer. The United States Pharmacopeia is doing a good job to create monographs for herbal products to allow the cGMPs to do their job. We need accrediting bodies that can place seals of quality on products. Good science based testing on quality is key. Clarity on what the FDA wants from industry is also

essential. Reporting safety issues is key to consumer confidence and will take a while to have an effect. The medical establishment also needs to become more aware of the natural remedies people are taking." (25)

The conversations with both of these industry professionals gave a clear picture of the growth of an infantile industry exploding from 4 to 25 billion in just 20 years. (33) It is almost as with the passing of DSHEA there was a rebirth of an industry and there was a clean slate to start from. It was not the clean slate that Commissioner Dr. Kessler had hoped for, but a new beginning of the supplement age here in the United States. As with any new industry, there are and will continue to be areas where many do not agree, especially within a regulated industry.

The first two interviews conducted represented a starting point to develop and formulate respective questions to representatives who must enforce or are impacted by the legislation of the DSHEA. To obtain different opinions on the regulation of dietary supplements, interviews were conducted with experts who are opposed and neutral on the Dietary Supplement Health and Education Act of 1994, including those who work for the regulatory agencies. The interview questions were developed around the background and expertise of each interviewee and therefore are not identical: however, core concepts of safety remained the same.

Dr. Peter Lurie

I was able to interview Dr. Peter Lurie, MPH of Public Citizen, a non-profit public interest group who lobby for the protection of the public to the federal government in various areas from energy to health care. Dr. Lurie is a medical researcher for Public Citizen and has been lobbying congress for a number of years concerning issues associated with DSHEA. He has been following the reports of adverse events associated with dietary supplements and

publishes his finding on www.worstpills.org, the Public Citizen website which researches pharmaceuticals and dietary supplements and presents their findings.

The following paragraph includes the questions and responses from our interview on October 15th, 2009.

Dr. Lurie, Public Citizen has been an outspoken critic of DSHEA for quite sometime, what would you like to see changed with the act?

DSHEA made it clear that the FDA had to regulate dietary supplements as foods rather than drugs. If these supplements have biochemical action in the body, they are acting like drugs and should be regulated accordingly. DSHEA tied the FDA's hands and raised the bar to remove products from the market. The requirement for a safety-based removal is high, and there is no requirement to demonstrate efficacy or safety prior to marketing. There are many people that are taking products that do absolutely nothing for them.

Do you feel the passing of cGMPs for the dietary supplement industry will have an impact on product quality and safety?

The cGMPs are long overdue. They have the potential to improve the quality of the products on the market. We have seen contaminated active pharmaceutical ingredient additions/adulterations, and no active ingredient in products over the past couple of years. The cGMPs will not do anything about the misleading promotion of these products and the inherent safety and effectiveness issues. Consumer fraud will continue, but the agency now has a stronger footing to remove products if there are cGMP regulations.

How can we improve the reporting of dietary supplement adverse events?

There is a severe under reporting of the adverse events associated with dietary supplements. The poison control centers would be a good place to start to expand under-reporting. The manufacturers need to be more educated on how to report these events as well. Patients need to be aware when taking any supplement that there may be a risk of a side effect.

Do you feel that companies should be required to register their products with the FDA before they are placed on the market? Would you support a user fee for the dietary supplement products to help pay for the various costs associated with regulations as with pharmaceuticals and medical devices?

There is absolutely no excuse for dietary supplement products to not be registered. I am opposed to user fees. I believe they cause a conflict of interest and create pressure for the rapid approval of products. It creates a pay to play mentality. User fees now fund the entire tobacco sector which is not a good thing. For drugs, FDA has to deliver a review by a specified time and industry gets to negotiate timelines. Product approval timelines should not be tied in with fees from industry.

What do you feel should be done with the promotion of dietary supplements? Do you feel the FTC does an adequate job policing the material put out by industry?

The FTC does very little. Dietary supplements are not a priority and the FTC treats these products as if they are a commodity. I believe these products should be in a different category. There is no way that the FTC can go up against the shear number of firms that are out there violating promotional rules. They need to

pick out a few representative violators and make an example of them. The gravity of the problem is beyond the grasp of the FTC alone.

Throughout the interview, Dr. Lurie explained that reform was going to have to approach from different angles to be effective.

"You cannot just go after one product at a time and expect success. There needs to be a whole paradigm shift in the way things are done. The FDA needs more effective enforcement tools and trained personnel to complete the tasks. Industry has to step up and say that we want to be responsible. Then we will start to see changes which will impact public safety. "

Dr. Vasilios "Bill" Frankos

Dr. Frankos is the current Director of Dietary Supplements Programs at FDA. To balance out the perspective from all sides of the issue I felt it was essential to get the statements from the Food and Drug Administration. In my interview with Dr. Frankos I focused on the facts surrounding dietary supplements, how things are perceived at the agency, and the direction of the agency in the future.

I was able to secure time with Dr. Frankos and the following questions and answers were recorded during a phone interview conducted on November 11, 2009:

How many employees currently work for the office of dietary supplements and of those employees how many are certified to conduct cGMP inspections?

The name of the office is actually Nutritional Products, and because of the way DSHEA is structured, you have quite a number of offices involved in dietary supplement regulations such as research and compliance. There is no good way

to put a number of the amount of people who work in the dietary supplement arena at the FDA. As far as the inspectors go, cGMP inspectors are not trained in dietary supplement cGMP inspections. They are trained to be cross functional and will therefore conduct more than just audits of supplement companies.

Do you think there should be an adverse event data base for consumers to research specific products or supplement active ingredients?

Yes, I do. In fact anyone can obtain information on a dietary supplement by doing a Freedom of Information request to the agency. The agency is in the process of creating something along the lines of the MedWatch database for drugs. It will take time but now that we have adverse event reporting in place the information should start flowing in, but it will take time. We are sometime from having this happen but it will come about in the future.

Has there been any thought to require manufacturers to list all specific ingredient amounts instead of the "Proprietary Blend" currently on the label of many dietary supplements?

What you see on the market is what has been agreed to. It was done that way to protect trade secrets from being stolen, however it is a risk to not have each ingredient listed out with how much the product contains. The only way to change this now is to create new legislation to change the current law. I am currently not aware of any currently going on that addresses this issue.

Has the FDA considered product registration or user fees?

Currently, there are no requirements to register individual products, but facilities must be registered. I know of two bills one in the house and one in the senate that

are dealing with this issue. They are both food safety bills. One bill I know is pushing for a user fee for firms that fail their first cGMP inspection and placing the repeat inspection cost burden upon the firm. Product registration is a ways off and I am not sure if these bills address that issue. They deal more with the clarification of what type of food manufacturing facility is registered. The bill would require the firm to be coded accordingly to designate whether it was a food or a dietary supplement manufacturer.

The FDA has started to focus on supplier quality issues in the drug arena, is there any push to extend the cGMPs to the supplement ingredient suppliers?

The dietary supplement cGMPs place the entire burden on the manufacturer, GMP ingredients have to be 100% identity tested prior to use. If a firm wishes to use a Certificate of Analysis, the firm must qualify the supplier accordingly. We need to work with what we finally have in place and go from there. There is no doubt in my mind that the cGMPs for dietary supplements will increase the safety of these products. Consumers will be confident knowing that they are getting what they pay for when purchasing a supplement and that they will be properly dosed.

Do you feel reform is needed to ensure safety of dietary supplements?

The FDA needs to continue to implement DSHEA to its fullest extent. It will take time for the cGMPs to have an effect but we will see improvement. Adverse event reporting had also improved greatly with dietary supplements; this is a whole new way of looking at safety of these products. It will allow us to better identify problem products.

Richard Cleland

Richard Cleland is an Assistant Director of the Division of Advertising Practices at the Federal Trade Commission. "The Division of Advertising Practices protects consumers from unfair or deceptive advertising and marketing practices that raise health and safety concerns, as well as those that cause economic injury. It brings law enforcement actions in federal district court to stop fraudulent advertising practices, coordinates FTC actions with federal and international law enforcement agencies sharing authority over health and safety products and services, and monitors advertising and marketing of alcohol, tobacco, violent entertainment media, and food to children. The Division also brings administrative lawsuits to stop unfair and deceptive advertising." (38) One of the agencies' main concerns is combating deceptive advertising of fraudulent cure-all claims for dietary supplements and weight loss products.

I spoke with Mr. Cleland via telephone and asked him a series of questions associated with the promotion of dietary supplements. The following paragraphs detail the questions and conversation which took place on January 22, 2010. Mr. Cleland stated that the conversation in no way reflected the opinion of the Federal Trade Commission; the statements made were of his own opinion.

Mr. Cleland, do you feel that the structure function claims used to promote dietary supplements mislead the consumer to believe the products have efficacy?

The public does not fully understand structure function claims. The public needs to make decisions about using supplements based on science rather than the claims. There is no question that DSHEA has been a boom for the supplement industry and there are

legitimate claims being used for products. There are also companies out there not following the rules when it comes to these claims.

How many dietary supplement firms were given violations for misleading claims in 2008?

This question has several layers. There were many warning letters issued to small, internet based companies based on a review of the claims on their websites, so a real number would be difficult to come up with. There is also a formal enforcement list which I will send to you. Many of those on the list are larger companies in which a civil investigation request has been made. In these cases, we generally rely on outside experts to evaluate the evidence and help us to decide whether a formal injunction or a cease and desist order is warranted. (Mr. Cleland provided a list of Dietary Supplement Advertising Cases. In 2008, sixteen major cases of advertising fraud were tried by the FTC in 2008. Over half of these cases were for misleading advertising of weight-loss products.)

The FTC requires claims about the efficacy of dietary supplements to be supported with "competent and reliable scientific evidence." How does the FTC define this statement and who decides if claims meet this requirement?

It is the job of the FTC to apply what is called a "balance test" to the claim. This is done on a case-by-case basis. We ask ourselves what level of evidence is required in the therapeutic area to make the claim. This is not rocket science. We see if the studies have been conducted and they are of sound science. Many companies cut corners and have no research and development departments. A majority of these companies using false

claims do not have the financial resources necessary to conduct the studies to support the claims.

What was the 2008 budget of the FTC to police dietary supplement advertising?

I can't really speak to dollar amounts, but we have approximately 25 full-time employees working in the health area. FTC enforcement focuses on product claims rather than product classification. The level of substantiation depends on the claim, not the product classification. Historically, our focus has been on weight loss products and companies making disease claims, rather than on structure function claims. There is such a vast pool of weight-loss products out in the market. Despite substantial efforts, it is a problem that is out of control. Many times these products don't work and some are contaminated with APIs. We see phenylpropanolamine which has an increased risk of stroke associated with it and subutramine which is also linked to heart problems and stroke.

How does the FTC receive notification of deceptive advertising associated with dietary supplement labeling?

The industry is somewhat self-monitoring. Many times competitors alert us to advertising issues. For whatever reason, consumers don't tend to file complaints about advertising. We regularly review sources such as newspapers, magazines, and especially infomercials. FTC looks for patterns associated with certain ingredients. Chances are if one company is promoting a product illegally, there are others out there following suit.

Do you feel that user fees would be a good way to increase the budget for policing deceptive advertising of dietary supplements?

Manufacturers should have to register with the FDA. I am not sure how user fees would enhance enforcement at this point. Right now there are no penalties. We need more oversight and a prior approval process for some kinds of products. Draconian penalties could be established for marketing without filing and the persons associated could be banned from marketing products for a certain time frame. We have an estimated 40,000 different dietary supplements on the market with about 1,000 new products coming out every year. It is impossible to police every product. There are enough resources to look at only about 3-4 dozen products every year. There is always an opportunity for deception. Effective deterrence requires significant monetary penalties and the perception that there is a high risk of getting caught. Right now, manufacturers have fairly good odds against getting caught. We strive to create a perception of strength in order to reduce the problems. In terms of resolution of the issues, it is a piece-meal issue. We have to attack different parts. In terms of the promotion of dietary supplements, advertising is not considered labeling. This issue needs to be looked at rationally. Areas of high incidence of fraud such as weight-loss products should be scrutinized for systemic solutions.

Rebecca Wright

Rebecca Wright is the editor of Nutraceuticals World magazine, a trade publication serving the dietary supplement, functional food and nutritional beverage industries. She has been with the magazine since 1999, taking over as editor in 2002. She interacts with the dietary supplement, functional food, and nutritional beverage industry on a regular basis to help provide an information resource to the general public. Her statements made are not the opinion of Nutraceutcials World magazine. They are her own opinions on the issues associated with

DSHEA. I spoke with Mrs. Wright via telephone on January 29, 2010. The following paragraphs detail the questions asked and the answers given by Mrs. Wright during the interview.

Mrs. Wright, what would you like to see changed with DSHEA?

The supplement industry for the most part is ethical. There is that small 5% of the industry that is not acting ethically. That 5% gives negative attention to the rest of the industry. The dietary supplements are improving consumer's health and research is moving forward. The FDA needs to enforce what is already on the books with DSHEA. The industry has been under enforced due to the fact that the FDA did not anticipate 30,000 products to be on the market. The ability to enforce will be the key.

Do you feel the passing of the updated regulations which require cGMPs to be followed by dietary supplement companies will have an impact on product quality and safety? If so, how?

The cGMPs are going to help but it will come down to enforcement. Companies will still slip through because of the limited resources. On paper the new regulations are great for the industry, but dietary supplements are way down on the priority list. Why would the government spend the money? Supplements will be safer and we will see a difference because of the adverse event reporting requirements and basic quality tests being performed.

What are your thoughts on improving the reporting of dietary supplement adverse events? (i.e. what does the FDA need to do to ensure compliance and education of the manufacturers ect.)

The law is very clear. Companies have been complacent and the FDA has been non-existent. Industry has become used to FDA doing nothing. This is not rocket science to figure out if you have a reportable adverse event. Responsibility should fall on the company marketing the product. FDA has clearly stated what is considered an adverse event. It (responsibly) is how you operate in a regulated industry.

Do you feel companies should be required to register their products with the FDA before they are placed on the market? Do you feel user fees prevent sub-standard companies from marketing products that are inferior? What cost would you deem reasonable for the FDA to charge if they did start charging for registration of products?

No, I do not feel user fees would solve any of the issues. Cheap entrance to the market makes small companies profitable. The interesting thing about the supplement industry is that it shows that innovation is not dead. Thousands of small companies make it in this business and that is what makes it great. It is a little piece of the American dream. Research is expensive and since it is very difficult to patent dietary supplements there is not a return on the investment. I do not see user fees helping prevent issues or improving safety.

How would you like to see a dietary supplement adverse event database for public use developed?

The FDA needs to get industry input on this issue and industry needs to participate. If supplement companies have nothing to hide, there should not be any push back from industry. Working together with industry leader will help to make this tool very effective for public use.

What in particular should be done with the promotion of dietary supplements? Do you feel the FTC does an adequate job of policing the material put out by industry?

The FTC is about as good in the regulation of promotional material for supplements as the FDA is at regulating; they do a pretty bad job. For example, the FTC came down hard on General Mills this year for their promotion of Cheerios cereal. There is not equal enforcement. Some producers lose big while others get away with everything they want. They are not equal enforcers and go after the bigger guys. They need to do something about the confusion of structure function claims as well. They are confusing to the consumer and even more difficult to understand from a acceptability perspective.

Do you feel it would be helpful to the industry to have the FDA create a GRAS (generally recognized as safe) list of dietary ingredients? Please elaborate on you answer on how this would or wouldn't be beneficial.

The term GRAS is usually reserved for food products and not dietary ingredients. Regardless, a list of dietary ingredients which were on the market before DSHEA would be very helpful. FDA also needs to clarify how to get a new dietary ingredient approved. As of now, the process is very vague and confusing. The real issue is they have very few resources to get this done.

Has Nutraceuticals World ever reported on unethical or substandard companies in the dietary supplement industry? How do you go about creating unbiased reports on the supplement industry at Nutraceuticals World?

Berkely Nutraceuticals was by far the most underhanded company I have come across while reporting on the industry. The CEO (Steve Warshak) was committing mail fraud by charging customers for products they didn't order and misleading consumers with a product that did nothing. They were originally fined 2.5 million in one case which was a slap on the wrist considering they made hundreds of millions off of the product. It was the cost of doing business to them. Eventually management was convicted on federal charges and the CEO was sent to prison.

Upon conclusion of the interview Mrs. Wright stated: "If DSHEA were repealed at this point it would mean the loss of hundreds of jobs in the United States. There are certain US Senators out there with dietary supplements in their crosshairs. As of now, there is no good way to get rid of DSHEA. The movement behind dietary supplements is to strong. Supplements have their role in health care, and they never get their due."

Chapter 5

Analysis, Proposals, and Conclusions

The passing of the DSHEA made it almost impossible for the FDA to monitor all that goes on within the supplement industry. In many cases FDA's hands are tied and nothing can be done. Recent passing of the mandatory reporting of serious adverse events was the first in few steps in the right direction for the supplement industry. Next, was the approval of the long awaited cGMPs for the dietary supplement industry. Good manufacturing practices were suggested by the Dietary Supplement task force in 1991, almost twenty years later cGMPs are finally a reality the industry will be facing. These two new regulatory statues will give the FDA more enforcement power over violators and an alternate route for removing problem products from the market.

The ultimate goal of a dietary supplement company should be to make a safe/effective product which benefits peoples' lives. The conclusions are based upon the interviews conducted and the researcher's assessment regarding balance of fairness between the operation of the industry and safety of the public. The data relevant to the changes identified by the author were analyzed using constant comparison method of analysis. Each item of data will be compared to the rest of the data to establish the conclusion categories. This process will create numeric data from the qualitative word data collected in the research interview process.

The data analysis used a methodical constant comparison process. Constant comparison can be defined as a method to analyze word data by creating categories that are scored and used to develop conclusions, themes, or hypotheses. (46) Questions were developed based upon a

general knowledge of what the author's findings were from independent research of issues surrounding dietary supplement regulations. For example, in reading works by Dan Hurly and Dr. Steven Barrett each author brought up the subject of adverse event reporting and the creation of a GRAS list for dietary supplement ingredients. Questions associated these key issues or "hypothetical conclusions" were created and are listed later on in this chapter. Categories were then extracted from the questions. These categories were then populated with key words, terms, or phrases which were recorded during the interview process. The key words or phrases were then scored on a scale of one to five based upon impact, positive (5) or negative (1), to the question associated with the category.

The two authors of DSHEA, Scott Bass and Loren Isrealsen, were not included in the analysis. The two authors of the regulations would not want to see change to their work and therefore it was determine that any categories which suggested change would be skewed by their input. In addition, even though interview questions were issued to both subjects, the interviews did not follow the questions which were asked. The responses given were more generalized talk of the history of dietary supplement regulations rather than direct answers to the questions provided. Additionally, a number of companies contacted for industry input to the subject matter did not respond to the request to be interviewed. This kept the number of actually participants analyzed to four. In addition, the key word, terms, or phrases (Appendix A) were decided upon by the author as well as the scoring of the phrases (Appendix B) based upon the impact questions.

The list below is the questions for each category upon which the interviewee's responses were scored against on a scale of one to five. (1-5) Additional information about the scale is listed in Appendix A. The questions are basic to help simplify the analysis. There are obvious

limitations to this type of scoring however it is widely accepted as a method of analysis for qualitative data. (44) A score of one would mean "no" or "does not agree". A score of three would mean a neutral stance on the question/subject. A score of five would indicate "yes" or "highly agrees" with the question. The analysis of this research was conducted by the author of the research, Matthew Rycyk. The context of the use of these phrases by the interviewees was taken into account when completing the scoring. There are limitations both to having the scoring done by the author and by persons outside of the research. There may be a perceived conflict of interest with the author completing the scoring. In addition, outside persons will not have the full context in which the phrases and comments were delivered during the interview as previously discussed in the semi-structured interview process in Chapter 3. The questions associated with each category are listed below.

Changes Needed (to regulations) - Does there need to be changes in the ways which dietary supplements are regulated?

cGMPs – Will the cGMPs for dietary supplements improve safety?

Adverse Events – Will a dietary supplement adverse event database be beneficial to consumer safety?

Product Registration – Should dietary supplements have to be registered with the FDA prior to their marketing?

Promotion of Supplements – Should there be something done about the way dietary supplements are promoted in the United States?

User Fees – Should user fees be attached to dietary supplements to support safety activities in the dietary supplement arena?

Gras List – Should the FDA create a GRAS list of dietary supplement ingredients on the market before October 15, 1994?

FDA/FTC – Does there need to be changes at the FDA/FTC in the way they approach dietary supplement regulation?

By interpreting the perceptions of a unique set of professionals regarding their experiences of the DSHEA Act, five ensuing propositions emerged from the data analysis. They include: increasing the funding to the FDA and FTC, creating an FDA generally recognized as safe ingredient list with corresponding monographs, requiring product registration, require user fees, adverse event data base. Each is individually explored and in greater depth to determine the degree or extent of these influences and recommendations for further study or potential implementation.

Increase the funding to FDA and FTC

In 2004, the federal government gave the Division of Dietary Supplements Programs 10 million dollars in operating funds to police a 20 billion dollar a year industry. (30) There were only 60 people working there at the time. The FDA was severely understaffed and underfunded to perform a job that was essential to the health of millions of people in the United States. The industry has exploded over the past 20 years and the workload has increase exponentially. Industry and anti-DSHEA advocacy interviewees held concern for the lack of funding to the Center for Food Science and Applied Nutrition (CFSAN) for use in regulation of dietary supplements. Each person interviewed stated there needed to be an increase in funding across the board to help support DSHEA.

The final issuance of cGMP regulations for the dietary supplements in 2007 created an additional workload that was not present in previous years. Personnel will have to be trained on inspections and this will take a number of new permanent positions. This in turn creates the need for additional permanent funding. The FDA must be willing to enforce the cGMPs throughout the industry or adulterated products will continue to be marketed in the United States. Dr. Hamburg has made it very clear that the FDA was very slow to act in the past and that this will no longer be the way in which business will be conducted. During my conversation with Scott Bass he stated that many firms will not be able to comply with the new cGMP regulations. "Many operations are mom and pop sort of places with strict operating budgets and minimal employees. The cGMP regulations will effectively put them out of business." To counter this fact, one would have to ask the general pubic if they feel safe knowing that a supplement which they are taking was produced in home or a warehouse. What these small manufacturers must realize is that they are dealing with a regulated industry where people's lives are at stake from the products they produce. Safety is the number one concern of the FDA, therefore sub-standard manufacturers should not be allowed to place product on the market. A set of solid, well-executed controls on manufacturing will allow a quality product to be consistently produced and the agency needs the money to enforce the cGMP regulations effectively.

The Federal Trade Commission (FTC) has done very little to enforce advertising regulations of dietary supplements since the passing of DSHEA. Director David Valadeck made it quite clear in a recent speech that the FTC is increasing enforcement efforts and aggressively pursuing compliance by dietary supplement firms to the guidelines. (37) They have had many other issues come in the way of putting dietary supplements at the top of the watch list in the past. Increased funding would allow the FTC to more effectively achieve this renewed effort.

As Dr. Lurie mentioned, “the FTC cannot police every supplement company”. The internet makes it almost impossible to shut down every violator. Finding key examples of violators and making examples of them to others will be essential in enforcing the advertising regulations associated with dietary supplements”. Loren Isrealsen and Scott Bass both stated that many companies are doing correct advertising and there are a small number of firms ruining things for others. A well-funded dietary supplements programs office at the FDA and FTC will be the basis for all other suggestions made in this research paper. Without the proper public funding, a change towards a safer industry cannot be made. An analysis of the constant comparison data gave an average score of 3.75, a slightly positive response from the research participants. Therefore, a recommendation is being made for changing the current budget through legislation to increase the funding to both FDA and FTC.

Create an FDA Generally Recognized As Safe Ingredient List with Corresponding Monographs

The constant comparison data was 3.1, a very neutral score. However, two of the four interviewees did not touch on the topic during their interviews. Since the passing of DSHEA, little has been done to create a list of dietary ingredients on the market prior to October 15, 1994. In addition, there is also not a list of commonly used or approved excipients for dietary supplements. The FDA needs to sit down with industry professionals and go over the data. There are many arguments out there as to why this could not be done, however through my research it seems necessary to get supplement manufacturers on the same page as the FDA. The FDA must also outline the process and scientific evidence it needs to have an ingredient placed on that list. Scott Bass stated “the United States Pharmacopoeia is doing a good job of creating monographs for well know supplements. (26) Dissolution and identity tests are an essential basis

of safety of a product and must be established for all active ingredients to ensure bioavailability. (31) The supplement industry needs some guidance of what FDA wants and an open dialogue must be established for any progress to be made.

Require product registration

The constant comparison data showed an average score of about 4.3. In 200, a review was done on complaints the FDA had received from 1994-1999 about dietary supplements. During this review, the FDA could not determine the manufacturer of 32 percent of the products involved in the reports. (30) Since that time, the Bioterrorism Act of 2002 was passed and now manufacturers are finally required to register with the FDA. (30) The FDA still does not know what products any of these companies produce and market. The changes in adverse event reporting after the Ephedra ban now require manufacturers to place an address or phone number on the labeling of the product. While these are steps in the right direction, in a regulated market, full disclosure of who makes what could prevent a public health disaster. Mr. Isrealsen and Mr. Bass were both against product registration when asked while Dr. Lurie stated "While this may have been acceptable in the past, in today's age of API adulteration and contaminated products, not registering with the agency is a public health disaster waiting to happen." In a recent speech delivered at the Council for Responsible Nutrition's Annual Symposium on October 22, 2009, Principal Deputy Commissioner Dr. Joshua Sharfstein suggested that "stricter enforcement of the requirement to notify FDA of the intent to market a new dietary ingredient might be a way to address the problem" (of safety). (37) Dr. Sharfstein also hinted at the completion of the guidance on what constitutes a new dietary ingredient subject to notification may be forthcoming. (37) The agency held a public hearing on this guidance in November of 2004 and

has been working on this for a number of years. (37) Hopefully this will be the pathway to full product registration by all dietary supplement manufacturers and marketers.

User Fees

The constant comparison data showed an average score of about 1.7, this supports a stance against user fees. In addition to requiring registration of products, it would be in the interest of the FDA to explore charging a nominal user fee to each new product. All persons interviewed were opposed to the idea of a user fee for different reasons. In fact, they were completely against the idea according to the constant comparison key word analysis. It is important to understand how the author of this research suggested use of these user fees would work and differ from drug or device user fees. The fee would not be in support of approval of the product in timely manner, rather support activities that are required to help keep the public safe such as consumer education, product testing, and an adverse event database. The FDA and industry can work together to determine the amount acceptable for each new product and base the amount on the size of the company as to not stifle the small businesses from entering into the industry. No firm enjoys paying to place a product on the market. The fact is that dietary supplements are a regulated industry. This sets the bar high for both industry and the regulatory agency involved. Public safety is a huge concern. While more public funding is a possibility, user fees would provide enough resources to add the manpower needed to conduct a safety review of each product coming to the market. This type of user fee would not place a "date" upon the product but be used as a means to support and police the products safety.

Implementing these changes would require direct legislation to amend DSHEA requiring product registration with CFSAN prior to marketing. This may take a number of years of

lobbying to produce enough votes to pass. It is difficult to see how registration would impact the industry. It is possible that unscrupulous companies will cease to exist purely because of this change. A majority of corporations will not risk placing a non-compliant product on the market if they know they will be under the direct watch of FDA and have to pay a fee to do so. The current law allows companies to subvert the system. Honest and truthful companies should have no issues with this legislation.

Dietary Supplements Adverse Event Data Base

The constant comparison score for this category question was 3.9, suggesting the subjects were in favor of having an adverse event database constructed by the FDA for dietary supplements. The FDA has made considerable efforts to present the proper information concerning dietary supplements in the hands of the consumers. Serious adverse events are now required to be reported to the FDA by supplement manufacturers as of December 1, 2007. Since that time, only a handful of reports have been submitted to the FDA compared to the multiple thousands of products on the market. The number of adverse event reports (AERs) is increasing every year. However, when compared to pharmaceutical drugs the supplement "AERs" are minuscule in comparison. The reports are usually not made by physicians. Poison control centers receive a majority of the adverse event reports. The unfortunate fact is that there is no communication to the FDA when these reports are made. Dr. Lurie stated "we see a large number of adverse events associated with dietary supplements go unreported." Loren Isrealsen is of the belief many adverse events will be reported that do not have anything to do with the dietary supplements that people are taking. There are many factors to consider when an adverse event is seen and physicians do not always know what they are seeing when an adverse reaction

presents in a patient. Proper investigational training on adverse event reporting should be conducted by the FDA and supported by industry.

Adverse event information which does get reported is buried deep within the FDA website. As stated before, there is no direct informational web page specific to dietary supplements. It would be difficult for a lay person to access the FDA website and conduct research on adverse events and drug/supplement interactions which are known to be associated with a specific dietary ingredient. The FDA does post some information in the "alerts" section of the dietary supplements web page. This information, while helpful, is not comprehensive or complete to someone researching a particular product. It is suggested by the author of this reserach that the FDA, possibly through public funding or the earlier proposed product registration user fees, create a complete active ingredient and product specific searchable serious adverse event data base for public use. The Public Citizen website, www.worstpill.org, has a fee associated with its use. Other websites such as www.fdable.com allow the user to search for dietary supplements, but fail to report information specific to the supplement. The user will almost always see the dietary supplement listed as a concurrent medication, not the primary cause of the adverse event.

A searchable website specific to adverse events associated with dietary supplements would allow the general public more information to then base their health decision of consuming a supplement. In the age of the internet, a solid source for accurate information on dietary supplements that has free access does not exist. The idea of consumer education initiative was originally suggested in the Dietary Supplement Task Force final report on page 62. (31) The real information from a source (FDA) which is unbiased and has no financial interest in the promotion of any product is essential to public health and safety of the public. Of all of the

suggestions made in this research, this one is the most critical and the most feasible to complete in a timely manner with limited resources. The database will allow consumers to complete effective research on their own before taking a dietary supplement. There would be no need for legislation to complete this type of project. The information is available; but needs to be compiled into a useable form for the lay person. After speaking with Dr. Frankos at FDA, a public database will most likely become a reality within the next couple of years.

Conclusions

DSHEA is one of the most interesting pieces of legislation passed in the last twenty years. The American public is very passionate about their dietary supplements. There is an overwhelming amount of support to keep the regulations exactly the way they were written in 1994. A grassroots movement around the dietary supplement supplement industry rises to the occasion any time the regulations are threatened with new legislation.

The dietary supplement industry has suffered because of the safety issues raised since the passing of DSHEA. These safety issues have created an environment of mistrust by the public of the dietary supplement industry. Similarly, the industry has always had a mistrust of the FDA. When researching DSHEA, it became apparent that the FDA has taken steps through the Dietary Supplement and Nonprescription Drug Consumer Protection Act (S. 3546) in 2006 and the finalization of the current good manufacturing practices for dietary supplements to improve safety. Dr. Frankos explained that these changes take time to see a reportable effect. "While it has been three years for adverse event reporting we are just now seeing more compliance from industry." An open dialogue between the two sides is essential to create a safer industry which embraces the regulations rather than fighting against them.

DSHEA was written in such a way to allow the FDA to regulate dietary supplements as foods. Since that time, the FDA has come to embrace supplement regulation as foods and have even gone as far as to defending this stance abroad to other countries. (34) The improvements of adverse event reporting and cGMPs will allow the agency to make vast improvements in safety; the public has just not seen the effects at this point. The full implementation of DSHEA from all angles will allow FDA to improve safety over time. This will not be an over night process and safety advocates should take note of this fact.

The industry has not wanted their products registered with FDA for a number of reasons. However, if industry is creating products which meet the regulations and are cGMP certified they should not have issues of complying. Allowing the FDA to know what products are produced by which manufacturers is standard regulatory practice amongst pharmaceuticals and medical device industry. It is a serious safety issue if the FDA cannot retrospectively track and identify source issues for products. An address on the label may not be enough to locate additional products that may be affected in a recall by the same manufacturer. Dietary supplements are part of a regulated industry. Industry must understand the safety of people's lives depend upon a chain of responsibility in the case of an adulterated product. Product registration with the FDA is the best way this can be accomplished. A constant comparison score of 4.33 shows that all who were interviewed were in favor of having dietary supplements registered before marketing.

User fees are a controversial topic. Dietary supplement user fee would not be the same as a traditional user fee for a pharmaceutical or medical device. The fee would be nominal compared to pharmaceutical and medical device fees and used to support new product registration, adverse event data base listing, and cGMP audits of facilities. This money would be

used to directly support safety activities associated with a manufacturer's product. User fees would have little impact on manufacturers total cost to bring a product to market but have a significant impact on over all product safety. The data from the research conducted does not support the user fee recommendation. User fees have a pay-to-play type of mentality associated with them and therefore many individuals perceive them as negative. In addition no company wants the cost of doing business to increase. Therefore, this recommendation of implementing user fees should be looked at last amongst the others recommended by this research.

In February of 2010, Senators John McCain and Byron Dorgan introduced the Dietary Supplement Safety Act of 2010. The bill would require dietary supplement facilities to provide FDA with information on supplements and their ingredients on an ongoing basis and would substantially alter the requirements applicable to new dietary ingredients. (42) Manufactures would essentially have to register their products. The bill also gives the FDA mandatory recall authority over dietary supplements and expands the adverse event reporting requirements. (42) One item of particular interest in this new bill is the proposed legislation to amend the definition of a "new dietary ingredient" and eliminate the references to October 15, 1994. The legislation authorizes the FDA to establish a list of "accepted dietary ingredients". Any dietary ingredient not on that list would be treated at a new dietary ingredient and subject to the 75-day premarket notification. This would effectively close the loop hole that allows manufacturers to avoid the premarket notification if the supplement "has been present in the food supply as an article used for food in a form in which the food has not been chemically altered". (42) In addition, manufacturers would have to keep a substantiation file with information relating to the claim that the dietary supplement will reasonably be expected to be safe. (43) This legislation would drastically alter the regulatory landscape of dietary supplements in the United States. Two of the

four recommendations made by this research are included in this new legislation. This research was conducted prior to the bill being introduced in the Senate of the United States. The alignment of this research's recommendations with the Dietary Supplement Safety Act of 2010 helps to support this research's recommendations even further.

I accept the hypothesis that reform is indeed needed to ensure the safety of the dietary supplement industry. It is obvious there are measures which need to be taken through legislation such as permanent funding increases, product registration, and a list of generally recognized as safe (GRAS) dietary ingredients. User fees should be considered but sufficient research should be conducted on this topic alone in order to better substantiate this change. However, my previous opinion that many legislative changes need to be enacted in order for safety to become a reality has changed immensely. I now believe very few changes need to be made to DSHEA. The straight forward recommendation of developing an adverse event database does not require legislation. These projects should be seriously considered to help DSHEA reach is full potential and implementation. They will be indirectly legislated through the funding of the FDA. Does total reform need to be weighed as an option? The answer to that question is no. In fact, I believe it would be very detrimental. Total reform of the industry would have a detrimental impact not only to the industry, but also consumer. The industry needs to let the FDA work effectively and understand that at this time efficacy is not the primary concern to the agency. They want to make sure each product is safe for consumption and not adulterated, which will be helped immensely by effective implementation of cGMPs. The dietary supplement industry is still in its infancy compared to other regulated products due to delays with the full implementation of DSHEA. The only direct change of DSHEA should include product registration and GRAS list recommendations proposed in the previous sections. This is

surprising to many reformists since they are calling for a complete change in DSHEA and asking for an overhaul of the entire Act. The time, effort, and money to initiate such reform would be a massive undertaking. As more time passes, we will see unsafe products disappearing from the shelves under the DSHEA regulations, as Dr. Hamburg explained "the FDA is just getting started on their safety initiative." (5) People need to trust that the DSHEA implementation measures that are taking place will start to have an effect in due time. The suggested changes to the regulations will strengthen these improvements and help to create consumer confidence in their dietary supplements which has not been seen in the past.

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APPENDICIES

Appendix A
Constant Comparison Key Word/Phrase Chart

Person Interviewed	**Key Word Categories**							
	Changes Needed	cGMPs	Adverse Events	Product Registration	Promotion of Supplements	User Fees	Gras List	FDA/ FTC
Dr. Peter Lurie, MPH (Public Citizen)	Foods, Efficacy, Act like drugs, hard to remove products	Overdue, improve quality, contamination issues, safety issues, consumer fraud, removed products	Severe under reporting, poison control, educate, patient awareness	No excuse for not having registration	Misleading, consumer fraud, FTC does little, not priority, number of supplement firms	Opposed, pay to play mentality, conflict of interest, no approval pathway	Not Applicable	Effective enforcement, trained personnel, changes which will impact public safety
Dr. Bill Frankos, M.S., Ph.D. (FDA)	Food safety bills, classification of facilities, implement DSHEA	Inspector not trained specific to supplements, failed inspections, burden on manufacturers, increase safety, confidence, properly dosed, 100% tested	FOI request AE info, along the lines with MedWatch, in the future, greatly improved, identify problems, new way of safety	No requirements, product registration is a ways off	Not Applicable	User fees for failed inspections	This is what has been agreed to, protection of trade secrets, New legislation	Nutritional products, a number of offices involved, implement DSHEA
Richard Cleland, J.D. (FTC)	Products don't work, effective deterrents against fraud	Contamination	Weight-loss products, contamination, thousands of new products	Manufacturers should register with FDA, 40,000 different dietary supplements	Public does not understand structure function claims, science rather than claims, companies not following the rules, balance test, case-by-case oversight, prior approval process	Not sure how user fees would help, no penalties	Not Applicable	Perception of strength at FDA and FTC
Rebecca Wright (Nutraceuticals World Magazine)	Most part ethical, supplements improve health, enforce what is in DSHEA, repeal would mean loss of jobs	Will come down to enforcement, way down on the priority list, limited resources	Supplements will be safer, quality testing, law is clear, responsibility on company, work with leaders, nothing to hide	Not Applicable	FTC dose a pretty bad job, not equal enforcement, confusion about structure function claims	No users fees, small companies need cheap entrance, innovation is not dead, user fees will not improve safety	Reserved for foods, would be very helpful, clarify a new dietary ingredient	Ability to enforce, did not anticipate forty thousand products, get industry input, clarify processes, not equal enforcers

Appendix B

Scored word phrases based upon a 1 to 5 scale. Scale=1 being of very little impact and 5 of significant impact to the issue of safety or changes needed as it relates to DSHEA surrounding the key word.

Person Interviewed	**Key Word Categories**							
	Changes Needed	cGMPs	Adverse Events	Product Registration	Promotion of Supplements	User Fees	Gras List	FDA/ FTC
Dr. Peter Lurie, MPH (Public Citizen)	3, 4, 5, 4= 16 16/4=4 **4**	5, 5, 4, 5, 5, 4=28 28/6=4.66 **4.66**	5, 3, 4=13 13/3=4.3 **4.3**	5=5 **5**	5, 5, 5, 3=18 18/4=4.5 **4.5**	1, 2, 1, 2=6 6/4=1.5 **1.5**	**NA**	5, 4, 5=14 14/3=4.6 **4.6**
Dr. Bill Frankos, M.S., Ph.D. (FDA)	3, 3, 5=11 11/3=3.6 **3.6**	2, 4, 5, 5, 5, 5=26 26/6=4.3 **4.3**	3, 5, 3=11 11/3=3.6 **3.6**	2, 3=5 5/2=2.5 **2.5**	**NA**	2 **2**	3, 2, 3=8 8/3=2.6 **2.6**	3, 1, 4=8 8/3=2.6 **2.6**
Richard Cleland, J.D. (FTC)	5, 5=10 10/2=5 **5**	5 **5**	3, 5, 4=12 12/3=4 **4**	5, 4=9 9/2=4.5 **4.5**	5, 4, 4, 3, 3, 5=24 24/6=4 **4**	1, 2=3 3/2=1.5 **1.5**	**NA**	4 **4**
Rebecca Wright (Nutraceuticals World Magazine)	3, 2, 4, 1=10 10/4=2.5 **2.5**	2, 1, 2=5 5/3=1.66 **1.66**	5, 4, 3, 4, 3, 3=22 22/6=3.66 **3.66**	**NA**	5, 4, 5=14 14/3=4.66 **4.66**	1, 2, 3, 1=7 7/4=1.75 **1.75**	2, 4, 5=11 11/3=3.6 **3.6**	4, 3, 3, 5, 4=19 19/5=3.8 **3.8**
Total Average of Interviewee's responses	**4+3.6+5+2.5=15.1** **15.1/4=** **3.775**	**4.66+4.3+5+1.66=15.62** **15.62/4=** **3.905**	**4.3+3.6+4+3.66=15.56** **15.56/4=** **3.89**	**5+2.5+4.5=13** **13/3=** **4.33**	**4.5+4+4.66=13.16** **13.16/3=** **4.39**	**1.5+2+1.5+1.75=6.75** **6.75/4=** **1.6875**	**2.6+3.6=6.2** **6.2/2=** **3.1**	**4.6+2.6+4+3.8=15** **15/4=** **3.75**