

NUTRI NEWS



**Douglas
Laboratories®**
Raising the Standard for Nutrition and Wellness™

Recent health and nutrition information from Douglas Laboratories

Special Edition

DOUGLAS LABORATORIES – RAISING THE STANDARD

Andrew Halpner, Ph.D.

While the topics of our NutriNews usually center on issues related to specific nutritional, health or disease conditions, it is appropriate every so often to review and update quality related concerns that surround the dietary supplement industry. This issue will focus on a number of product quality issues and offer independent test results covering topics such as: unsafe lead levels in calcium products, pesticides in Korean ginseng, heavy metal contamination in fish oil, and the presence of magnesium stearate in products. In the absence of independent testing to verify the purity of content, product claims are meaningless.

There exists some confusion surrounding the dietary supplement industry, leading to some public misperceptions. The industry is often viewed as having a lack of quality, standards, and accountability in the manufacturing and sale of dietary supplements. Some feel that the same standards that apply to drugs should apply to dietary supplements, and since those standards are currently different, the quality of dietary supplements should always be in question. At times, the media even portrays the industry as unfocused and unregulated and is critical of many products that reach the store shelves.

While it is true that dietary supplements are not drugs or over-the-counter medications, they are regulated, although differently from the way the Food and Drug Administration (FDA) regulates pharmaceuticals. Without getting into a cumbersome review of regulatory law, it is important to understand a number of key concepts.

The Dietary Supplement Health and Education Act (DSHEA) of 1994 treats dietary supplements as a category of food, and is therefore regulated in a manner similar to conventional foods. According to the law, the definition of a dietary supplement is as follows: "A product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin; a mineral; an herb or other botanical; an

amino acid; a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any ingredient described...." DSHEA also specifies rigorous guidelines regarding the manner in which products must be labeled and how certain claims can appear on the packaging of supplements.

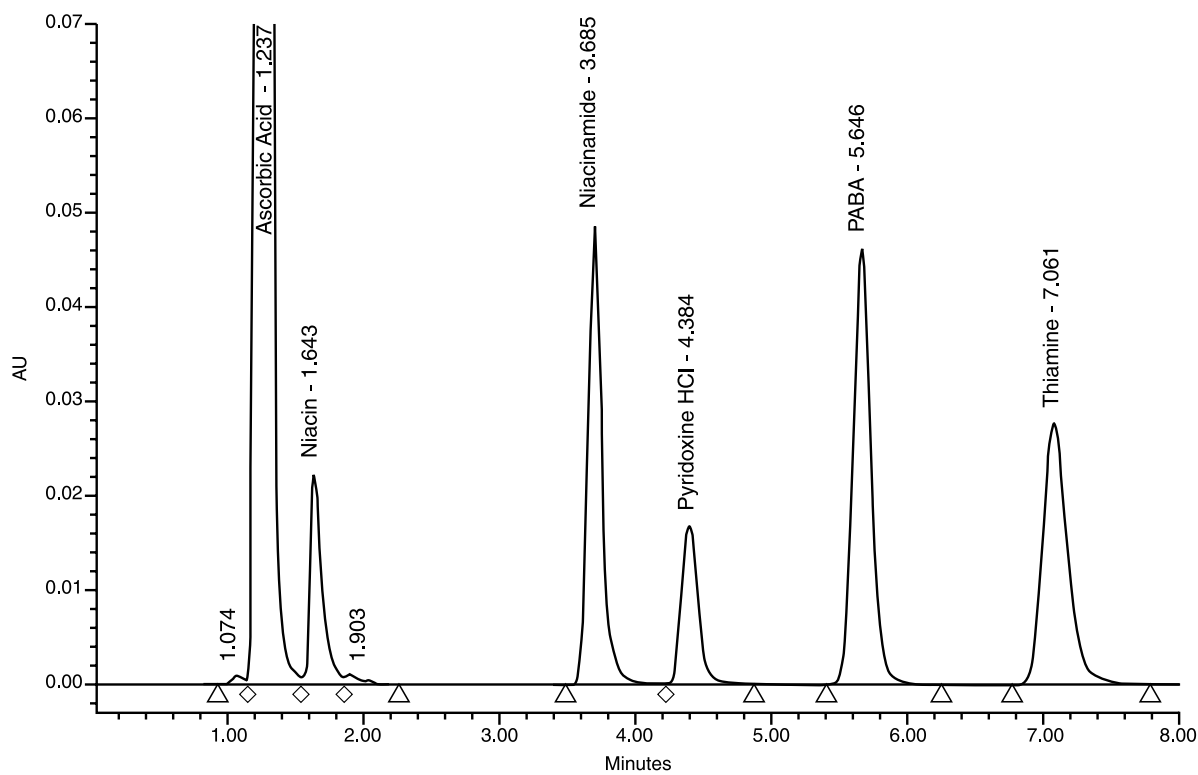
While the law is specific with respect to many issues, some areas have been left gray. For instance, there is considerable argument over how a "dietary substance" or "constituent" should be defined. One particularly important yet brief area of DSHEA deals with good manufacturing practices (GMPs) – loosely defined as a set of regulations and procedures that detail how every step in a manufacturing facility is to be documented and executed – specific to the dietary supplement industry. Unfortunately, the DSHEA does not specify what the GMPs are; it only mandates that the government should propose certain regulations. While the FDA is working toward defining GMPs for the dietary supplement industry, the current absence of industry-specific GMPs contributes to the mistaken impression that manufacturing practices are unregulated. However, the industry's top tier companies, as well as trade organizations, have developed extremely well-defined GMPs that are as stringent as, if not more so, than the expected GMP rules from the FDA.

At Douglas Laboratories, detailed written standard operating procedures (SOPs) dictate what must occur in the manufacturing facility to ensure product quality. Our GMPs and SOPs guarantee that every step of production is accountable and conforms to or exceeds industry standards. While no one is sure what the government will require when the final GMPs are issued, we are confident that our current procedures and attention to detail will exceed any new regulations.

HPLC Chromatogram Chart

Sample Information

Product Number	Ultra Preventive® III (#7454)	Lot Number	1200252
Vial	2	Run Time	8.0 Minutes
Injection	1	Date Acquired	1/5/01 10:35:54 AM
Injection Volume	20.00 ul	Date Processed	1/10/01 9:20:46 AM



Peak Results

	Name	RT	Area	Height	USP Resolution	USP Tailing
1		1.074	5314	862		8.165594e-001
2	Ascorbic Acid	1.237	9390717	2387025	1.121368e+000	1.292135e+000
3	Niacin	1.643	142600	22645	2.952641e+000	1.736264e+000
4		1.903	8624	1034		
5	Niacinamide	3.685	358445	47985		1.270258e+000
6	Pyridoxine HCl	4.384	140233	17088	3.422373e+000	1.270709e+000
7	PABA	5.646	421004	46283	5.525256e+000	1.152209e+000
8	Thiamine	7.061	359252	27914	4.879178e+000	1.299934e+000

Quality Measures

Testing and retesting is key to the production of a quality product. Our in-house testing laboratories include Microbiology, Physical Properties Testing and Analytical Analysis. Raw materials and finished products are tested in our microbiology lab for yeast, mold, E coli, and other potential bacterial contaminants to ensure the product meets and or exceeds the requirements of the United States Pharmacopoeia (USP). Our physical properties laboratory tests for parameters such as hardness, disintegration, and dissolution to ensure that tablets and capsules disintegrate and release their nutrients properly. Our analytical lab is outfitted with extremely sophisticated high performance liquid chromatography (HPLC) systems for the measurement of various vitamins and herbal components. Figure 1 shows an HPLC chromatogram from one of our products during the testing procedure. Our analytical lab also contains an inductively coupled plasma (ICP) instrument for the analysis of minerals and heavy metals. In all steps of the manufacturing process, there are quality control cross-checking procedures in which more than one person checks for accuracy and consistency at each phase of production. Douglas Laboratories also uses a cold process manufacturing technique so the product is not exposed to heat or moisture, as can occur during wet granulation manufacturing techniques, to achieve content uniformity and preserve potency within each batch of product. Such meticulous attention to quality produces nutritional supplements that meet or exceed label claims.

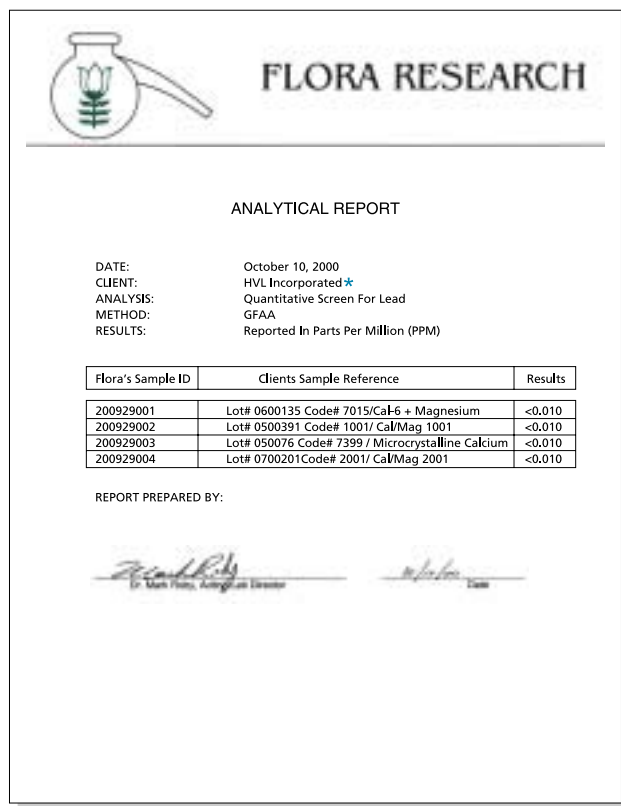
Lead and Calcium Supplements

While great lengths are taken to ensure that supplements are produced of the highest quality and contain what is stated on the label, the finished product is only as good as the starting material, something which recent media attention fails to take into account. As is often the case, one issue in particular that has been in the news recently is the potential contamination of calcium supplements with lead. Much of this concern stems from a 1993 report in the American Journal of Public Health that stated 25% of calcium products tested exceeded the FDA's allowable limit of 6 mcg of lead/day. This, however, is not really surprising as calcium is often found together with lead in the earth's crust as well as in the human body, especially in bone.

Fortunately, with better mining and extraction techniques, the industry has been able to effectively remove much of the lead that is associated with calcium. A more recent analysis of lead in calcium supplements published in **The Journal of the American Medical Association** last year reported much improved results. Of 21 over-the-counter calcium products tested, 13 had lead levels below the limit of detection. Of those products that did contain detectable levels of lead, all were below the FDA's limit of 6 mcg of lead per day. In an editorial accompanying the **JAMA** report, Robert Heaney, M.D. states, "a luncheon of mixed salad greens and a glass of Chardonnay will contain 10 to 50 times as much lead as could be ingested in a typical calcium tablet." So, contrary to some



Figure 1



*HVL Incorporated is the parent company of Douglas Laboratories.

sensationalistic media reports about out-of-date studies taken out-of-context, in general it appears that the consumption of lead from food and beverages exceeds the amount of lead that would be consumed as a result of taking calcium supplements.

While 6 mcg of lead per day is the limit that has been set by the FDA, California has imposed an even more stringent level of not more than 0.5 mcg/day as part of their Proposition 65 regulations. Although some feel that this level is unreasonably low, all calcium products sold in California need to adhere to this limit (for a calcium supplement, the limit is actually 1.5 mcg/day as the law allows for 1 mcg of lead/1,000 mg of elemental calcium to be naturally occurring).

As a result of this publicity and resulting public concern, Douglas Laboratories has subjected our calcium products to in-house and independent testing of lead levels. While it is not possible to show results for every product we offer, we selected a number of our more popular products, including 7015-Cal-6 + Magnesium, 1001-Cal/Mag 1001, 2001-Cal/Mag 2001, and 7399-Microcrystalline Calcium. As can be seen in Figure 1, the lead levels in all of these


products were below the limits of quantitation and well below the California and FDA limits as measured by the atomic absorption graphite furnace method, a highly sensitive technique. As a customer of Douglas Laboratories, you can be assured that our products containing calcium are safe, efficacious and exceed industry standards.

Korean Ginseng and Pesticides

Another issue receiving media attention is the presence of pesticides in Korean ginseng. Again, it is important to see the facts behind the sensationalism. Much of the Korean ginseng that enters this country from Asia has been treated with pesticides at some point during its life. The EPA has set limits on acceptable levels for certain pesticides, but not all. For example, although the European Pharmacopoeia and USP have set a limit of 1 ppm for quintozone (a commonly used fungicide also known as pentachloronitrobenzene), this limit does not apply to the US dietary supplement market. Consequently, the current acceptable limit for quintozone is zero. Given this growing concern about quintozone and other pesticides, a number of suppliers now offer pesticide-free ginseng, which has undergone a special manufacturing process to remove any pesticides that may be present in the product. However, not all supplement companies are aware of this issue, and therefore do not offer a pesticide-free ginseng. Douglas Laboratories offers only



Figure 2



FLORA RESEARCH



ANALYTICAL REPORT

DATE: August 18, 2000
CLIENT: HVL Incorporated*
CLIENT'S SAMPLE DESCRIPTION: Korean Ginseng Root Powder Lot #13129
FLORA'S SAMPLE ID: 200815022
ANALYSIS: Chlorinated Pesticides Screen
Limit of Quantitation: 10 ppb

Compound	Results
PCB (pentachlorobenzene)	N/D
TCA (Tetrachloroaniline)	N/D
HCB (Hexachlorobenzene)	N/D
Alpha-BHC	N/D
PCNB (Pentachloronitrobenzene)	N/D
Lindane	N/D
Beta-BHC	N/D
PCA (Pentachloroaniline)	N/D
Delta-BHC	N/D
PCTA (Pentachlorothioanisole)	N/D

N/D=Not Detected

REPORT PREPARED BY:



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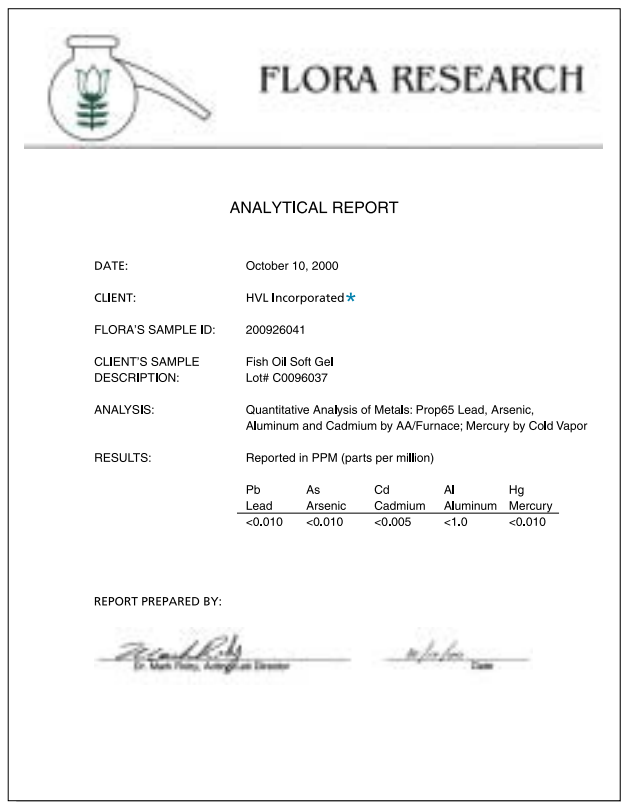
pesticide-free Korean ginseng. If you are not currently purchasing your Korean ginseng from Douglas, ask the company from which you purchase your product to provide you with the analytical results from their ginseng demonstrating it is free of pesticide contamination. Figure 2 shows a complete independent analysis of pesticides in one of our Korean ginseng raw materials in which no pesticides are detectable. Douglas Laboratories does not accept any ginseng material in which any of these pesticides are above the limit of detection.



Fish Oil

There has been a growing concern about the potential for fish oil products to be contaminated with heavy metals. This is usually a concern when the fish used in the manufacture of the oil have been taken from polluted waters. However, fish oil that is prepared from fish taken from clean, unpolluted water and processed via a method involving distillation is generally free from heavy metal contamination. Most of the fish from which our fish oil products are made originate from the cold waters of the south Atlantic and south Pacific oceans. We recently tested a number of our fish oil-containing products for heavy metal contamination. Figure 3 shows the independent test results from our product 7980-DEPA, and Figure 4 shows results from product 7040-EPA/GLA Forte. Lead, arsenic, cadmium, aluminum, and mercury were all below their respective limits of quantitation, meaning that they could not be detected and are free from heavy metal contamination.

Figure 3



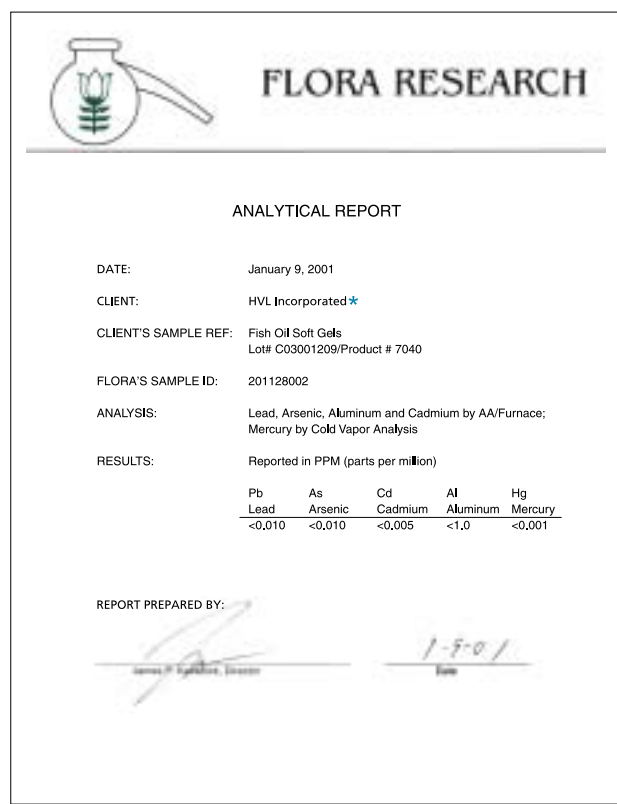
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Magnesium Stearate

The issue of magnesium stearate having deleterious properties as an excipient in dietary supplements is a topic that has existed for quite some time; however, the data to support that point of view is weak at best. The issue of magnesium stearate is a classic example of how repeated marketing efforts can appear to carry more weight than actual scientific data. To separate fact from fiction, it is important to understand the role of excipients in product manufacture.

Excipients are non-active ingredients that assist the physical process of making the tablets and capsules. Certain physical properties of a supplement's active ingredients (e.g., fluffy, hygroscopic, sticky, etc.) require certain excipients to assist the product flow through the encapsulating or tableting machinery. The excipients most commonly employed are cellulose (derived from trees), silica,

Figure 4



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and magnesium stearate (derived from plant sources), each playing a unique role in assisting proper capsule or tablet production. Douglas Laboratories adheres to U.S. Pharmacopoeia and National Formulary monographs that outline their accepted use.

The use of excipients also helps ensure proper content uniformity (consistent amounts of active ingredients from capsule to capsule). Additionally, an excipient may be necessary if the quantity of active ingredient is small. For example, a capsule containing 400 µg folic acid, and 10 mg vitamin B6 would obviously not fill the volume of even a small capsule. Consequently, an excipient will be used to manufacture a well-filled capsule. While certain ingredients have the physical properties to run without excipients; they are definitely not the majority of compounds used in the dietary supplement industry.

The following are some of the false claims made regarding magnesium stearate use:

False Claim #1) *“Stearates used as lubricants to speed up the production of nearly all supplements clearly decrease the absorption of nutrients and may be toxic and immunosuppressive”*

This statement is clearly inflammatory and ignores existing science. A thorough search of the literature fails to uncover any peer-reviewed, published data (or any published data for that matter) demonstrating that the presence of magnesium stearate in a dietary supplement decreases absorption. The work most commonly cited in support of this argument appears in the journal **Pharmaceutical Technology** which investigated the effect of magnesium stearate on the dissolution of a drug from a capsule. First, it should be pointed out that dissolution cannot be used in place of actual absorption. Making the claim that an effect on dissolution will directly result in a change in absorption is not true. Many factors regulate the absorption of nutrients, not simply the laboratory assessment of dissolution.

The study demonstrated that in the presence of croscopovidone (a starch-based excipient) and lactose, magnesium stearate had an effect of the dissolution on the drug. However, the study also demonstrated that in the absence of lactose and starch... “interactions between drug and excipients were essentially absent.” In another study published in the **Journal of Pharmaceutical Sciences**, it was concluded that when the powder was free of non-pregelatinized corn starch, “...drug dissolution was not affected when thoroughly mixed with magnesium stearate.” The authors conclude that magnesium stearate may interact with starch and lactose in a way that affects dissolution. Consequently, products that are free from lactose and non-pregelatinized starch are not relevant to these experiments. In fact, most dietary supplement formulations are free of lactose, which is more typically used in drug formulations. This important point is often conveniently excluded from the argument against magnesium stearate. Furthermore, it should be kept in mind that even in the work that did include lactose and starch in the presence of a drug, absorption was not studied. For all that is known, a slightly slower rate of dissolution might enhance absorption. Making the statement that, “stearates...clearly decrease the absorption of nutrients...” is therefore completely unfounded.

False Claim #2) *“Magnesium stearate is a toxic, hazardous substance.” Companies that manufacture and transport magnesium stearate must file a Material Safety Data Sheet with the Environmental Protection Agency because magnesium stearate is classified as a hazardous substance”*

Here is another example of how the truth can be contorted to make magnesium stearate appear hazardous. While magnesium stearate does come with a Material Safety Data Sheet (MSDS), so does every other nutrient with which we work. Even the water we use in our laboratory is accompanied by an MSDS. The presence of an MSDS is not a result of the EPA stating a material is “toxic”: rather an MSDS contains important information regarding how to handle the material, what precautions to take in the event of a spill or a fire, and similar safety concerns.

False Claim #3) *“Inhalation of magnesium stearate may irritate the respiratory tract”*

This statement is factually correct and does appear on the MSDS for magnesium stearate. However, this statement appears on most every MSDS we receive and is a typical statement made for many ingredients. For example, the MSDS for *Siberian ginseng* states, “...may cause eye or respiratory irritation upon contact.”

Can you guess where this statement comes from? “Causes irritation on contact with the eye. Expected to cause coughing, wheezing, and general respiratory tract irritation after inhalation of vapors or dust. Treat as toxic if swallowed.” These statements appear on the MSDS for *quercetin*, a natural bioflavonoid. Based solely on this logic, quercetin should be immediately removed from all products. For that matter, just about everything would have to be removed to the point that nothing could ever be considered safe for ingestion.

False Claim #4) *“Magnesium stearate in supplements has immunosuppressive effects.”*

This is another attempt to take science drastically out of context, in this case work from the journal **Immunology**. In this study the investigators treated T cells growing in culture with stearic acid. The investigators found that stearic acid suppresses T cell function. Those that argue against the use of magnesium stearate reference these findings to support their position. However, this is taking the

work grossly out of context. In this study the authors had designed a special cell culture model where the cells would selectively take up stearic acid bound to an albumin complex. Additionally, these cells were deprived of all exogenous unsaturated fatty acids. These unique conditions can in no way be generalized to *in vivo* human situations. Moreover, the body converts stearic acid to oleic acid once ingested, so cells are exposed to relatively small amounts of stearic acid, and certainly nothing resembling the conditions in the experiment cited takes place in normal human physiology. In fact, the author of the T-cell study, Dr. Thomas Buttke, in private correspondence had the following to say with respect to the claims being made about magnesium stearate. **"...the bulletin which cites our 1990 Immunology publication is misleading and inaccurate in several respects..... while I am usually pleased by recognition afforded our research, in this instance I would prefer that [they] not try to use our studies to support their ill-founded claims."**

While making the generalization that magnesium stearate is detrimental to dietary supplement preparations may be a successful marketing technique, it is irresponsible and unsupported by scientific data. This type of borrowing science from one field of study and using it out of context does a disservice to science in general, and the supplement industry in particular. Unfortunately, when misinformation such as this becomes pervasive, science must prevail. Decades of scientific data do indicate that magnesium stearate is an inert plant-source substance. It is widely used in the manufacturing process of many nutritional supplements to ensure proper encapsulation and tablet formation and to help facilitate the blending of multiple ingredients to provide consistent content within each serving.

Our Commitment to the Well-Being of Our Customers

"Raising the Standard for Nutrition and Wellness" is not just our slogan, but the driving force behind our commitment to quality. Douglas Laboratories routinely evaluates the latest research and evolving technologies to incorporate into the development and manufacture of new and existing products. We are committed to continually improve our products and processes to ensure your patients receive the finest nutritional supplements available anywhere. Scientific facts support the safety and quality of our production processes. We hope that this information clarifies any issues relating to the science, quality and regulatory aspects of dietary supplements and provides an expanded insight into their manufacture and safety.

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Dr. Halpner received his Ph.D. in Nutrition from Tufts University School of Nutrition Science and Policy. His extensive research and interests focus around antioxidant nutrients, including their interactions and ability to prevent and treat age-related degenerative diseases. Dr. Halpner is Director of Product Development and Technical Services for Douglas Laboratories®.

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