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DIRECTOR'S MESSAGE



Spring has sprung in the DC area, and as quickly as it arrived and brought an end to what felt like a long winter, a lush green canopy has now replaced the vibrant pop of colors from Mother Nature's bounty of flowers and trees, and much of the country is at this point looking at some much needed rain – and unfortunately in some cases floods. Mother Nature is a powerful lady and at the SupplySide East show a few weeks ago, I was reminded of that fact.

I heard from many an aloe supplier on the show floor that the winter weather and particularly the freeze that occurred several months ago that dipped pretty far down into Mexico has caused some significant issues with aloe vera crops and many are looking for leaves en masse. Though no one's said we're looking at an absolute catastrophe, it's certainly no surprise that we've been receiving a great deal of interest from locations such as Greece, Iraq, Iran, and similar areas for information and assistance in setting up cultivation and processing operations. The damage freezes can do to the viability of the crops is certainly significant.

On the good news front, Virgo Publishing has inked an agreement with the IASC to co-produce and hold the "IASC 2011 aloe vera Symposium: Science, Regulations & Market Opportunities" on October 14, 2011 as part of the SupplySide West trade show in Las Vegas. This will be the first IASC science symposium in some years – and I for one and very excited that not only will we have what will be an excellent event full of information from experts on a variety of topics of interest to the industry, but also that with Virgo as a partner we're sure to see strong attendance and receive excellent support.

From the regulatory and science standpoint – we released an Update recently on our meeting with the FDA in May, the development and passing of a quality standard for aloe vera raw materials, and new studies that are on the way from the NTP/FDA – and the clear message that industry needs to produce safety/toxicology data via studies of its own. I also attended the April peer review meeting of the NTP 2-year study, and provided IASC comments. We continue to monitor all channels of the media actively and have thankfully seen very little pickup.

In a nutshell – it continues to be a busy time for the organization and the industry and we continue to have challenges to face and things to look forward to.

And, as always, members are encouraged to contact the IASC with any questions.

Devon Powell
Executive Director



Europe and is now demanding a hefty price for the assignment of the mark to the U.S. company. We strongly advise clients to ignore offers of this kind and, if they are indeed interested in obtaining protection of their trademark in Europe, to instead apply for a Common Market Trademark (CTM) registration, which will provide the owner with the actual, legal right to exclusive use of the trademark in all countries within the European Union.

Other companies we have encountered contact trademark owners to purportedly “alert” them that someone else is imminently about to register an Internet domain name containing their trademark in a given foreign nation. For example, the message might “alert” the owner of the trademark USU that another company is about to take out the domain name www.usu.cn in China. The message then proceeds to offer to register that foreign domain name for the trademark owner. Although these companies generally seem to actually provide the advertised service of domain name registration, these services are provided at an immense mark-up that far exceeds the cost of using a legitimate trademark firm located in that country. Moreover, there is not necessarily any need for a U.S. company to take out a domain name in a foreign country where the U.S. company has no plans to do business. For those of our clients who do plan to do business in a foreign country, we regularly work with foreign counsel to obtain both the relevant foreign domain names and the official trademark registration for our client’s mark in that country.

Other offers that trademark owners may receive come from so-called U.S. trademark- service companies offering to perform trademark prosecution, and maintenance services such as filing renewals for trademark registrations and responding to office actions on pending trademark applications. The prices for these proposed services are most often substantially higher than a typical trademark law firm’s standard fee. Moreover, it has been our experience that such companies often offer substandard services that may result in harm to the trademarks in question.

It is telling that solicitations such as those described above are always sent directly to the trademark owners, rather than to the attorney of record whose

contact information is also listed in the USPTO’s public records. We remind clients that any legitimate inquiry would be directed to the attorney listed on the trademark record. If you receive any query regarding your trademarks that looks official but is directed to you rather than your trademark counsel, please assume it is a scam and send it on to your counsel. Ullman, Shapiro & Ullman’s trademark staff will be pleased to answer your questions regarding any such query.

[Charles Knull](#) is Trademark Counsel at Ullman, Shapiro & Ullman LLP; [Linda Dougherty](#) is Associate at the firm.

“Inside Law” is an Inside Aloe: Online exclusive column by IASC General Counsel Ullman, Shapiro & Ullman. Ullman, Shapiro & Ullman is a New York, N.Y.-based law firm that specializes in legal issues in the dietary supplement and natural products industry (www.usulaw.com).



IASC Board Approves Quality Standard for Raw Materials; Meets with FDA

May 23, 2011 - Last week the IASC Board of Director’s approved a [quality standard](#) for aloe vera raw materials that covers items such as polysaccharide content, isocitrate (also often called “whole leaf maker” or WLM), contaminants, and other constituents typically found within the botanical. “This is a notable accomplishment for the organization,” said IASC Executive Director, Devon Powell, “having this standard will raise the bar on the aloe industry as well as further enhance the IASC certification program and further distinguish those products meeting the program requirements and legitimately displaying the seal.”

[The quality standard](#) will be incorporated in the aloe vera leaf juice monograph still under development by the American Herbal Pharmacopeia (AHP). Interest in having the same information coordinated with a United States Pharmacopeia (USP) monograph also continues to be discussed. The standard was developed over the

that the clock is ticking. As at the 2009 meeting, FDA again questioned the characterization of aloe vera products available in the marketplace and made it clear that information was something it expected industry to provide. A marketplace survey has been discussed and is expected to be produced and delivered to the membership for response shortly.

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■ aloe vera industry needs to identify
■ and characterize the ingredients
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■ anecdotal or unqualified evidence."

"This is what the NTP studies done to date have concluded: there is something in the aloe vera material they tested that caused carcinomas in rats," said Powell. "Even though that material (non-decolorized whole leaf extract of aloe barbadensis Miller - a non-carbon filtered or unpurified material) is not what industry sells - it's not yet known what caused the issue in the rats, as they studied the broadest possible material. This new study is designed to find that out and the first thing they will be trying to see is if it's the aloe latex. I've seen biology info from toxicologists that say it's likely the aloin. At this point, however, we don't know definitively - as an industry - what "it" is or "they are" that caused the problem in the rats - and that's the problem. We need to prove it using the same toxicological methodologies."

Prior to adopting the quality standard, a report on the meeting was provided to the board which then

discussed how to address the concerns and questions raised by the agency, particularly in regards to the safety studies that would likely need to be conducted by the industry. Steps that were identified by the board in the process included:

- ◆ Conducting a market survey of raw material suppliers & possibly finished product suppliers to identify the primary ingredients used in marketplace goods for oral consumption, currently believed to be decolorized inner leaf juice, decolorized whole leaf juice, and non-decolorized inner leaf juice. Provide such information to the agency to better assist them in understanding the ingredients currently available in the marketplace and reduce confusion.
- ◆ Characterize the ingredients identified by the market survey using the now adopted quality standard, supplier CofA's, IASC certification program data, and other means. This information will be useful both for assisting the agency in reducing confusion about the ingredient in the marketplace, but also will help IASC in determining what ingredients to look at for any safety studies to be conducted.
- ◆ Collect and review any toxicological or safety study data. Members will be asked to provide any toxicological or safety study data on the ingredients identified via the market survey for review and to determine if any of that data will be able to be made of use.
- ◆ Determination of any industry-developed safety studies that need to be conducted and obtain proposals. IASC has retained Life Sciences Research Organization (LSRO) to assist in the review of any current studies as well as develop any safety studies that are deemed necessary.

"The IASC and its members take consumer safety very seriously and IASC aloe vera marketers don't sell products that are unsafe," said Powell. "Even so, the FDA made it clear that the aloe vera industry needs to identify and characterize the ingredients in the marketplace definitively, and actively produce or develop toxicological data to clearly demonstrate safety and build a body of evidence for use against any

forthcoming toxicological studies, and cannot rely on anecdotal or unqualified evidence. As the FDA said - the clock is ticking. We've been given what amounts to fair warning. It's time to act."



SPECIAL TOPICS

The Rising of the Green Sun

By Casey Adams, PhD.

This article in a nutshell

- ◆ The cereal grasses
- ◆ Aloe vera
- ◆ Green sprouts
- ◆ Sea grasses
- ◆ Spirulina
- ◆ Chlorella
- ◆ Haematococcus and astaxanthin
- ◆ Blue-green algae from Klamath Lake
- ◆ Fermented green foods
- ◆ The rise of the green sun

While sales of many supplements have fallen or remained flat during the past few years, greenfood supplements have continued their steady rise into the hearts and minds—make that stomachs and bloodstreams—of consumers.

According to data provided by Jennifer Fuller of SPINS, Inc., combined retail channel wheat grass and barley grass sales are up 13% over last year (52 weeks ending February 20), the chlorophyll/chlorella category is up more than 13%, and spirulina sales are up almost 7% over last year. More important, mass-market sales are up significantly. Wheat/barley grasses were up 19% in the conventional channel, chlorophyll/chlorella sales were up more than 21%, and other algae sales have more than doubled from a year ago.

This growth in the mass-market channel during times when many have tightened their spending illustrates the value proposition made by greenfoods. "Quality

green food supplements are important to the consumer because greenfoods are the one dietary area lacking in almost everyone's diet," said Ron Seibold, president and CEO, Lawrence, Kan.-based Pines International.

Greenfoods provide practically every nutrient imaginable, including enzymes, minerals, trace elements, and essential and non-essential amino acids, vitamins, antioxidants, and various phytonutrients. "Most greenfoods provide at least 1,000 nutrients that are lacking in many modern diets," explained Dave Sandoval, founder of greenfoods supplier Organic By Nature, Inc., in Long Beach, Calif. "Greenfoods are not like isolated synthetic nutrients. They are ancient foods with qualities to feed the world."

A big benefit of greenfoods is their alkalinity. "Acidosis is a major health concern for the vast majority of western nations because of lifestyle and diet choices. Industrialized diets include acidic or acidifying elements such as meat, cereals, coffee, tea, alcohol and sugars, and not enough alkaline foods such as vegetables," said Jeff Wuagneux, president and CEO, RFI Ingredients, in Blauvelt, N.Y., supplier of a range of greenfoods. "Countering acidification is as simple as reducing the acids the body is taking in, and increasing alkaline foods or alkaline supplements."

Much of this alkalinity comes from greenfoods' bioavailable mineral content. "Soil-based minerals are metallic, and plant-derived minerals are colloidal," said Elmer Heinrich, president of Tulsa Oklahoma's Liquid Assets, Inc., a supplier of plant-derived minerals. "Metallic minerals are hydrophobic in nature, possessing a positive electrical charge. Plant derived minerals have been transformed by the plant into non-metallic, water-soluble colloidal minerals that are easier for the body to assimilate."

Cereal Grasses

Wheat grass is the young grass of the wheat species, *Triticum aestivum*. In addition to a plethora of vitamins, minerals, amino acids, phytonutrients, and metabolic enzymes—including superoxide dismutase and cytochrome oxidase—wheat grass maintains up to 70% chlorophyll.

Early research by Dr. Charles Schnabel, Dr. George Kohler, and Dr. A.I. Virtanen in the 1925-1950 era found that cereal grasses like wheatgrass achieved their highest nutrient content at around 18 days—right before the first jointing.

Pines International, a wheat grass producer, continues to use this science to this day. “We grow and harvest our product in the manner used in the foundational research,” commented Pines’ Seibold, referring to Schnabel and Kohler’s 25 years of research. The Pines company launched its products in the United States in 1977. “We were the company that coined the term green food,” Seibold added.

Post-harvest handling is critical. “The method used to remove the moisture from the wheat grass is state of the art and is the most gentle possible, resulting in wheat grass with maximum levels of enzymes, vitamins, beta-carotene, chlorophyll and phytonutrients,” Seibold explained.

Wheat grass can increase blood hemoglobin levels. Wheat grass tablets decreased blood transfusion needs by 25% among 20 children requiring frequent blood transfusions in a recent study.

Sales of wheatgrass supplements have continued to grow steadily for Pines, according to Seibold. “Our sales have had solid or better growth every year for the past two decades, even with recent economic news, probably because people recognize the nutrition-per-penny value of wheat grass,” he said.

Barley grass powders are also enjoying steady growth. “We’ve continued to grow over the last few years, and so far, 2011 is growing even faster,” said Bill Atkinson of Green Foods Corporation, in Oxnard, Calif. Green Foods Corp. introduced its barley grass products to Japan in 1969 and to the United States in 1979.

“Yoshihide Hagiwara, MD, was the first to develop the process of producing juice powder from greenfoods,” Atkinson claims. “He held the patent for the process for 30 years.” Before finding his healthy stride in the greenfoods industry, Hagiwara ran a leading Japanese pharmaceutical company.

“Our barley grass is grown on the North Pacific island of Keshu in fertile volcanic soil, giving our grass optimal nutrients,” Atkinson continued.

In fact, research has found that barley grass is a potent free-radical scavenger, significantly reduces total cholesterol and LDL-cholesterol, and inhibits LDL oxidation.

As Atkinson pointed out, the nutrient and antioxidant potency may have something to do with this: “Our barley grass juice powder has at least 14 vitamins, 18 amino acids, 15 enzymes, 10 antioxidants, 18 minerals, and 75 trace elements.”

Greenfoods Corporation juices its barley first. “The juice is then gently spray-dried at low temperatures to retain nutrients and enzymes,” Atkinson explained. “Because enzymes are hydrolases, they are retained during juicing and spray-drying. They hold their activity when rehydrated.”

Customers can find both dried leaf powders and juice powders in the marketplace. “Juice powder nutrients are a lot more bioavailable because the plant cell walls are broken down during juicing,” Atkinson said, adding, “Leaf powder is dried first, leaving more fiber content, but since some of the nutrients are trapped inside the cell walls, they are less [bio]available.”

Another cereal grass rising to prominence is Kamut grass. According to the Kamut International company of Missoula, Mont., the Kamut brand khorasan wheat has higher protein levels than most wheat varieties, and contains higher zinc, selenium and magnesium content. Selenium is known for stimulating glutathione activity.

The Kamut variety is also being preserved for future generations. “The Kamut trademark guarantees the preservation of the ancient khorasan wheat variety: it will never be hybridized or genetically modified,” said Trevor Blyth, CEO of Kamut International, owner of the Kamut trademark. “The variety will always be grown certified organic with high standards for nutrition and purity.”

Consumers and manufacturers are beginning to recognize these benefits. “In 2010, we saw total annual

growth of almost 40%, which was due in large part to consumers looking for high quality nutritious alternatives to modern wheat,” Blyth said.

One Kamut license-holder and producer of Kamut grass powders is Liquidry of Abraham, Utah. “Our Kamut juice powders and other cereal grasses are produced using our proprietary Ever-Raw process,” says Liquidry’s president, Elend LeBaron. “This enables us to classify our juice powders as ‘raw’ because processing temperatures never exceed 106 degrees Fahrenheit.”

LeBaron has watched his company’s sales of Kamut and other cereal grass powders soar during the past few years. In fact, he said, “Our biggest growth has occurred since the recession began.”

Aloe Vera

While aloe has long been known for its skin-irritation and wound-healing abilities, science on its internal use is still emerging.

According to Jeff Barrie of Aloecorp, Lacey, Wash., “Consumers drink *Aloe vera* for gastrointestinal health, immune support and to help maintain healthy cardiovascular systems. Another growing use for aloe is for nutricosmetics.”

Aloe may also help prevent kidney stones. A study published in the *Journal of the Thailand Medical Association* found that 200 grams of fresh aloe gel a day significantly decreased urinary oxalate excretion.

In addition, a study from London’s Queen Mary School of Medicine on 44 active ulcerated colitis patients found that internal aloe use resulted in clinical improvement. And double-blind, randomized research using Aloecorp’s Qmatrix-processed aloe has shown that it reduces oxidative stress markers and stimulates the immune system.

Reaching a significant milestone, Aloecorp recently completed GRAS (Generally Recognized As Safe) certification for its aloe. “We are very excited about the future since more and more consumers are discovering the benefits of drinking *Aloe vera*,” Barrie commented.

Green Sprouts

Virtually ignored for many years as a supplement, sprout powders are now becoming heralded as nutritional greenfood powerhouses. “Sprouts have exponential nutritional value, far greater than those of the seeds or the fully grown plants,” said Steven Lattey, director of raw materials for Moab, Utah, sprout and cereal grass juice powders supplier, The Synergy Company.

This was confirmed in 1970s experiments by former Hippocrates Health Institute Director of Research Viktoras Kulvinskis, M.S. Kulvinskis, who found that ascorbic acid levels in soybean sprouts increased from zero to 103 milligrams per 100 grams by day six—about the ascorbic acid content found in lime juice. These levels fall off significantly within days.

Each plant has a different nutrient peak. Ascorbic acid content in broad bean sprouts—used to cure scurvy during World War I—peaks in three days, after which the levels fall off.

“The sprout appears to produce greater antioxidant levels as a defense mechanism against threats from the soil,” Lattey explained.

The Synergy Company supplies a host of sprouts, ranging from bean sprouts to wheat grass sprouts. Cruciferous sprouts such as broccoli and cabbage are also becoming more popular, according to Lattey. “These provide an extraordinary class of nutrients called glucosinolates. Glucosinolates yield sulfur compounds and indole-3 carbinols. These have been studied for their anti-tumor and anti-inflammatory benefits,” he said.

Nutrient availability requires exacting sprouting techniques. “Proper sprouting requires accurate seed selection because unsprouted seeds spoil overall nutrient content,” Lattey offered. “Most seeds have about a 30% germination rate. We hand select specialty heirloom seeds that have a 98% germination rate.”

The Synergy Company uses a special milling and flash-freezing technique to preserve the nutrient content of its sprout powders. “We utilize an oxygen barrier process

that helps prevent oxidation and nutrient loss,” added Lattey.

Sea Grasses

Kelps might be called “seaweeds,” but these phytonutrient powerhouses are anything but “weeds.” About 1,500 species of sea kelps flourish, many in the North Pacific and North Atlantic oceans.

Most kelps are stationary, and sustainably harvested in the wild. This means they must be allowed to regrow to guarantee future harvests. “Wild harvested kelp can be certified organic under the U.S. Department of Agriculture National Organic Program Regulation §205.207, which addresses wild-crop harvesting practices,” says Bill Wolf, president of kelp producer Thorvin, Inc., New Castle, Va. “Organic Certified’ kelp from Thorvin is harvested sustainably in a pristine Icelandic fjord.”

Thorvin’s *Ascophyllum nodosum* kelp contains an impressive array of vitamins—more than many vegetables. “Kelp delivers over 60 essential minerals,

amino acids, vitamins and growth promoters,” said Wolf.

Most kelps also contain fucoidan, a sulfated polysaccharide. Laboratory studies have indicated fucoidan has anti-tumor, anticoagulant and anti-angiogenic effects. It down-regulates Th2 (inhibiting allergic response), inhibits beta-amyloid formation (implicated in Alzheimer’s), inhibits proteinuria in Heymann nephritis and decreases artery platelet deposits.

Preserving these nutrients in kelp is an important consideration. “Thorvin kelp is carefully dried at low temperatures using geothermal energy, which preserves its nutrient density,” Wolf explained.

Draco Natural Products of San Jose, Calif., is another producer of kelp and other seaweeds. “We extract our sea vegetables using a water-only extraction process. Our extraction process is a closed system using proprietary technology to break open plant cell walls to release the actives,” said Brien Quirk, Draco’s director of Research

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& Development. “Water is superior in extracting compounds insoluble in a hydroalcoholic extraction, such as polysaccharides, flavonoid glycosides, and more polar compounds.”

Draco produces powders of kelp, sargassi seaweed, *Undaria pinnatifida*, sea palm, and others.

Thorvin’s and Draco’s sea vegetable sales have continued to rise, even through the recession. “Thorvin’s sales have grown at an annualized average of more than 20% over the last decade—with higher growth anticipated this year. We sell well in excess of 1000 tons per year,” Wolf offered.

Spirulina

Spirulina use dates back to the Aztecs. A good source of carotenoids, vitamins (including vegan B12 according to independent laboratory tests), and minerals, spirulina contains all essential and most non-essential amino acids, with up to 65% protein by weight. It also contains antioxidant phytonutrients such as zeaxanthin, myxoxanthophyll, and lutein. “Spirulina contains a high level of antioxidant carotenoids, vitamins, and minerals. It also contains a unique blue pigment, phycobiliprotein, which is only found in blue-green algae,” says Gerald Cysewski, PhD, founder and chief science officer, Hawaii-based Cyanotech.

“These phycocyanins in spirulina provide significant anti-inflammatory and antioxidant effects,” says Chief Technology Officer Amha Belay, PhD, of Earthrise in Irvine, Calif.

More specifically, Cysewski said, “Phycobiliproteins have been shown to protect both the liver and kidney from toxins. In addition, spirulina contains anti-viral compounds and compounds that stimulate the immune system.”

The two leading U.S. spirulina producers are Earthrise and Cyanotech. Earthrise produces its spirulina in sun-drenched Southern California, while Cyanotech produces theirs on the Big Island of Hawaii.

Both grow spirulina in huge volumes. According to Dr. Belay, Earthrise’s produces more than 400 tons per year,

with demand continuing to increase.

Both producers are concerned about the quality of imported spirulinas, which is why cultivation techniques are tantamount. “Our ponds are all lined, and have no contact with soil,” said Dr. Belay. “Soil contact increases contaminants and heavy metals in the final product. [Companies] should assure their spirulina is coming from a lined pond with no soil contact.”

“We are one of few spirulina producers with a Hazard Analysis Critical Control Point (HACCP) program,” Belay continued. “Our company and Cyanotech are also the only spirulina producers that have achieved Food and Drug Administration GRAS status. Other spirulina producers may have internally developed GRAS documentation, but not necessarily reviewed by FDA.”

Belay suggests commercial buyers test their spirulina periodically. “Our tests have shown that some imported spirulinas have higher quantities of heavy metals and insect fragments and reduced nutrient profiles,” he said. Cyanotech recently announced a laboratory study finding one offshore source had seven times the lead of its spirulina.

“Hawaiian spirulina has been evolving into a superior strain over the past 25 years. Continuous cultivation, along with a patented Ocean Chill Drying method, helps protect the fragile nutrients in Hawaiian spirulina,” Dr. Cysewski noted.

Hawaiian spirulina was used in a new study from the University of California-Davis on 30 adults over 50 years of age. After 12 weeks of 3000 milligrams of spirulina per day, patients were tested for hemoglobin concentration and mean corpuscular hemoglobin levels, which were higher among the subjects. IDO (indoleamine 2,3-dioxygenase) enzyme activity—a sign of increased immune function—was also higher among the subjects.

E3Live, Klamath Falls, Ore., has developed a (patent pending) process to extract the phycocyanins from spirulina. “Our process utilizes mechanical extraction methods rather than the synthetic extraction used elsewhere,” says E3Live’s CEO Tamera Campbell. The

translucent blue E3Live product is called Blue Magic. “This is the only natural blue-coloring food dye available, and we are in the process of completing our GRAS certification,” she added.

Both Earthrise and Cyanotech report that their spirulina sales have continued their steady rise. In fact, Cyanotech’s President and CEO Brent Bailey announced recently that its branded spirulina sales increased 25% last quarter.

Chlorella

More than 800 published studies have verified the safety and efficacy of *Chlorella pyrenoidosa*. Chlorella’s reputation of drawing out heavy metals and other toxins make it a favorite among health practitioners.

Chlorella maintains considerable vitamins, minerals, and phytonutrients—including chlorella growth factor (CGF), known to stimulate cell growth. It is also a complete protein, with about 60% protein by weight

and every essential and non-essential amino acid. Clinical studies have shown that chlorella stimulates T-cell and B-cell activity and contributes to the improvement of fibromyalgia, ulcerative colitis, and hypertension. Another study showed that chlorella increases IgA levels and lowers dioxin levels in breast milk.

Torrance, Calif.-based Sun Chlorella is a leading producer. “We harvest our product in fresh water under pristine conditions to ensure maximum quality,” says Guinevere Lynn, director of business development. “One of the most unique qualities of chlorella is its ability to replicate at an extremely high rate.”

“As chlorella multiplies, it is transferred into progressively larger outdoor pools,” Lynn continued. “Eventually, it is placed in the largest of the culturing pools, 36 meters in diameter. The water originates from 3,000-meter-high mountains. The chlorella is constantly stirred to ensure maximum sunlight exposure. Repeated centrifuging separates out foreign elements.”

Aloecorp’s Qmatrix® Aloe Now Has GRAS Status!

The Generally Recognized as Safe (GRAS) status of Aloecorp’s Qmatrix aloe has been affirmed by an independent panel of scientific experts for use in a broad range of foods and beverages.

We invite you to visit our website at www.aloecorp.com for more information.



www.Aloecorp.com 800-458-ALOE (2563)

Chlorella's tough cell wall must be broken down mechanically to allow this nutrient's bioavailability. "Chlorella cannot be fully digested in its native form by human digestive enzymes," explains Lynn. "Our patented process pulverizes this tough outer cell wall, allowing maximum bioavailability and digestibility of the nutrients."

Haematococcus and Astaxanthin

Another rising microalga is *Haematococcus pluvialis*, known for its high astaxanthin content. "Astaxanthin is a carotenoid pigment similar to beta-carotene—and the most abundant carotenoid in the marine environment," said Cyanotech's Cysewski.

"Astaxanthin has been shown to be the most powerful natural antioxidant known and also has anti-inflammatory properties. As such, it can address a number of health issues, including joint and muscle soreness, cardiovascular health, eye health, and even skin health, as it can protect against damage by UV radiation," Cysewski added.

Charles DePrince, president and CEO of astaxanthin producer Fuji Health Science, Mt. Laurel, N.J., said his company has sponsored more than 50 research studies on astaxanthin during the past 10 years. "The strongest bodies of research include eye fatigue, cardiovascular health and muscle endurance," he stated.

"When *Haematococcus* becomes stressed it begins to accumulate large amounts of astaxanthin," Dr. Cysewski said.

"It produces high levels of astaxanthin just prior to entering its hibernation state," DePrince added. "The natural purpose of the astaxanthin content within the alga is to protect it from lipid per-oxidation."

In contrast to Cyanotech's outdoor cultivation, Fuji's cultivation process consists of fully enclosed biosystems located in Gustavsberg, Sweden. "Following cultivation, the alga is harvested, dried and extracted via a solvent-free, CO₂ supercritical process," noted Mr. DePrince. Both Fuji and Cyanotech report continued sales growth through the recession. "We have seen a sharp increase in the growth of sales over the past six months in response to what we feel is the reaching of critical mass in

research and resulting recognition of the value of natural astaxanthin," Mr. DePrince opined.

Further, Cysewski added, "Health practitioners and consumers are beginning to learn about the many positive benefits of astaxanthin." Cyanotech announced 40% sales growth in branded astaxanthin last quarter.

Blue-Green Algae from Klamath Lake

Aphanizomenon flos-aquae or AFA, grows on the pristine waters of Klamath Lake in Oregon. Commercial AFA harvesting began in the early 1980s.

"The rich volcanic Klamath Lake renders our product a good source of protein, with all the essential and non-essential amino acids, as well as many vitamins, minerals, and phytonutrients," said Campbell of E3Live. AFA contains about 60% protein by weight, and at least 58 minerals at ppm levels, along with significant chlorophyll content.

One of the more exciting phytonutrient compounds discovered in AFA is phenylethylamine (PEA). "PEA is often called the 'love molecule,' because it increases positive moods. It is found in foods like chocolate—though AFA contains significantly more than chocolate," explains Campbell.

E3Live recently developed a product with enhanced levels of PEA, called BrainON. "BrainON improves brain function and mood, and neuro-enhancement overall," Campbell said.

"E3Live's flagship products are fresh frozen, leaving nutrients biologically available. But for long-term shelf life we use a proprietary method of low-heat drying called Hydro-drying, which retains the viability of nutrients and enzymes within the product," she said.

E3Live's AFA sales have been steadily increasing despite the recession. Campbell says the company's customers use it in functional beverages, snacks, greenfood mixes, and others.

Fermented Greenfoods

This significant effort among greenfood producers to retain nutrients through innovative processing

techniques continues to render innovation. One recent innovation is fermentation.

RFI Ingredients has developed a unique system of greenfood fermentation. “Fermentation naturally breaks down the nutrients in greenfoods by the action of beneficial microorganisms. The fermented greenfoods are easier to digest, have more nutrients, and are preserved longer,” said Wuagneux. “We can ferment numerous ingredients, from cereal grasses to fruits and vegetables. In addition to improved nutrient bioavailability, these fermented greens have the added benefit of probiotic bacteria, which help restore and balance intestinal microflora.”

The Rise of the Green Sun

The green sun is still rising on the market, with plenty of upward sky to traverse. This comes from the fact that greenfoods resolve fundamental dietary deficiencies. “Even after 35 years of spreading the message of “eat more green,” the average modern diet is still lacking in these foods. Retailers need to look at greenfoods as a staple in the diet. They are foundation supplements that customers should be using before they use anything else,” Pine’s Seibold concluded.

A longtime advocate of greenfoods, Casey Adams is a California naturopath with a PhD in Natural Health Sciences, and the author of several books on natural health. Adams is also the president of Realnatural, Inc. and can be contacted at ca@caseadams.com.

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classification relies heavily on commercial practice and understandings, not just the indications given on labels, literature, or otherwise. The court reiterated that it was not required to determine how effectively CS functioned as an OA pain reliever, but rather, found it sufficient that the marketplace, among other factors, recognized CS as a therapeutic substance. In *Inabata Specialty*, the court recognized that the classification of CS depended upon the “use” of that product and thus took into consideration each of the factors to determine what that use is in the United States at, or immediately prior to, the date of importation of CS.

■ “Although this article focuses on issues concerning fish oil supplements, there are many additional herbal and dietary supplements that may be incorrectly classified and subject to Customs duties.”

The same argument that was made in *Inabata Specialty* can be made for fish oil supplements. There are provisions in the tariff for fish oil supplements that are more relevant and would allow the fish oil supplements to be imported into the United States, free of duty regardless of the country of origin or manufacture.

The industry and the commercial understanding of consumers that purchase fish oil supplements is clear—use of the fish oil supplements is intended to both treat and prevent various and specific ailments and diseases. There is a body of scientific evidence that supports the fact that fish oil supplements are prepared, bought, and sold for such purposes, and not simply for general health and well being. This is strong evidence to support the marketing and public perception of the efficacy of fish oil supplements and, concurrently, that fish oil supplements are medicaments and should be treated and classified as such. With the importation of

fish oil supplements increasing from year to year, the savings in duty upon a successful appeal to Customs or, failing that, the Court of International Trade, would be substantial and may potentially result in an ocean of savings.

Although this article focuses on issues concerning fish oil supplements, there are many additional herbal and dietary supplements that may be incorrectly classified and subject to Customs duties. Manufacturers and importers would be well served to learn more about the classification and country of origin marking of herbal and dietary supplements and whether such provisions apply to their products.

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The Herbal Products Consumer Revealed

In spite of a maturing market for dietary supplements, the opportunities for herbs and botanical products remain very positive, according to Steve French, managing partner at the Natural Marketing Institute, a leading business consulting and market research firm. It’s just a matter of supplying products that meet consumers’ evolving needs.

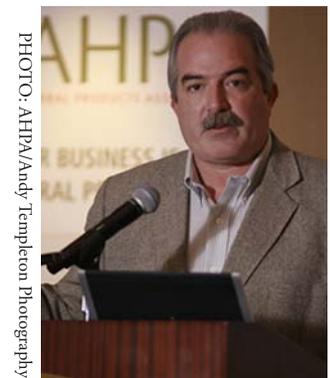


PHOTO: AHPA/Andy Templeton Photography

Steve French

French shared data from his firm’s extensive Health &

■ "35 percent of herb users preferred to take their supplements in forms other than pills and capsules. This was up from 23 percent in 2003."

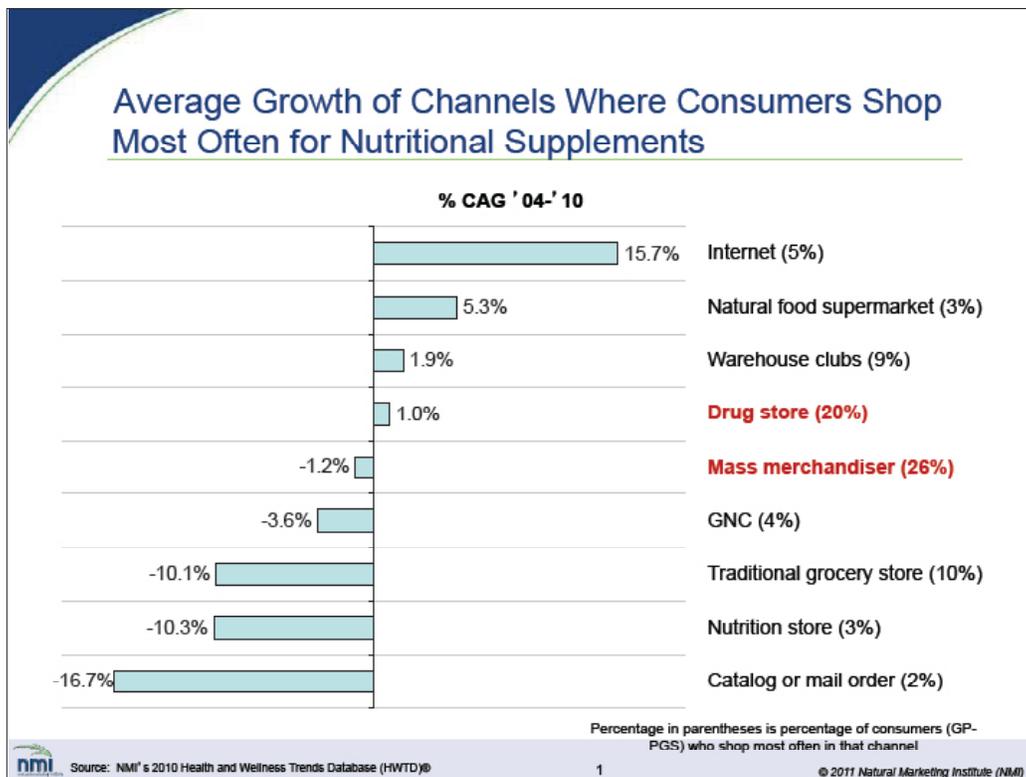
Wellness Trends Database, a comprehensive resource for measuring consumer attitudes, behavior patterns, product usage, lifestyles, and demographics, during a presentation to the American Herbal Products Association (AHPA) membership at the annual member meeting on March 10, held at Natural Products Expo West in Anaheim, Calif.

Despite showing a recent decline in new product offerings due to the recession, the data, drawn from the

company's most recent consumer interviews, also shows that consumers of herbal supplement products are what French characterized as an "intense group," because they say that herbs and supplements are "extremely to very important" in maintaining a healthy, balanced lifestyle. Baby boomers are more likely to take herbs than the general population and are the most avid consumers of the products compared with other age groups.

French noted that the primary driver of herbal product usage is "to promote overall health" and that secondary drivers include the promotion of immunity, treatment of specific health issues, improved digestion, and increased energy.

Noting the high level of lapsed usage of aloe, echinacea, and ginseng, French said that the perceived effectiveness of the entire supplement category was still an issue with consumers, with only 31 percent of herb users perceiving the effectiveness of herbal products as "very effective." Still, condition-prevention concerns continue to drive usage among herb users.



The four channels showing nutritional supplement growth from 2004 through 2010 were the Internet, natural foods supermarkets, warehouse clubs, and drug stores. Drug stores and mass merchandisers combined to serve 46 percent of all supplement shoppers. SOURCE: NMI's 2010 Health and Wellness Trends Database.

French showed that 35 percent of herb users preferred to take their supplements in forms other than pills and capsules. This was up from 23 percent in 2003. According to French, this was a "wake-up call" to supplement manufacturers, especially as boomers and the overall population continue to age and may have difficulty taking pills and capsules. He cited quick-dissolve strips, fizzing tablets, and chewables as growth opportunities. Another opportunity for manufacturers is the increased consumer desire for supplements from natural, organic, and vegetarian sources, according to the NMI research.

issues surrounding botanicals that fielded questions from the audience.

The ICSB conference is supported by a cooperative agreement between the NCNPR and the Center for Food Safety and Applied Nutrition (CFSAN) at the US Food and Drug Administration. It is co-sponsored by the Shanghai Institute of Materia Medica/CAS, China; the Council of Scientific and Industrial Research (CSIR - India); the Ministry of Indigenous Medicine, Sri Lanka; the American Society of Pharmacognosy; the Society for Medicinal Plant and Natural Product Research; and the Korean Society of Pharmacognosy. Unfortunately, several FDA employees of CFSAN were unable to travel due to funding uncertainty. The conference was well attended nonetheless!

The European Situation

Opening the first session, “Current Status of Science and Regulations of Botanicals in Europe,” Gerhard Franz, PhD, from the Universität Regensburg in Regensburg, Germany, gave a talk titled “Up-to-Date Development of Herbal Drugs and Herbal Drug Preparations in the European Pharmacopoeia.” He discussed terminology differences, pointing out that the terms *herbal drug* and *herbal drug preparations* are in the 2010 *European Pharmacopoeia 7.0* (EP), while the term *botanical* is not officially used. He also mentioned that the EP standards apply to all medicines regardless of origin and that the 2010 two-volume EP that was implemented last year contains 2,300 monographs and now has a separate “Herbal Drugs and Herbal Drug Preparations” section. These monographs total 178 and 80 examples, respectively, in the seventh edition, which is up from 123 and 61 monographs in the sixth edition. The increase is partly due to the addition of 15 monographs on Traditional Chinese Medicines (TCM).

Dr. Franz pointed out that the United States doesn't yet have observer status at the European Pharmacopoeia Commission, and he discussed the situation for herbal drugs in Europe by reviewing the regulatory categories of Traditional Herbal Drugs and New, or Well Established, Herbal Medicinal Products. He clarified that *herbal drug* is synonymous with the term *herbal substance* as used by the European Community

legislation on Herbal Medicinal Products.

He also explained that herbal preparations can be obtained by subjecting herbal drugs to processes such as extractions and include extracts, essential oils, and expressed juices. He noted that powdered herbs are much less used now than herbal extracts, and he defined Standardized, Quantified and Other extracts, and native vs. not-native extracts, being those that also contain technical excipients.

Dr. Franz defined Standardized extracts as extracts that have constituents with known therapeutic activity, such as a belladonna leaf dry extract, while Quantified extracts have a defined range of active markers, such as St. John's wort extracts. A third category, Other extracts, were defined as essentially process defined but which may have a defined minimum of analytical markers as with some valerian extracts. Regarding the 75 TCM-candidate monographs for the EP, it was conceded that not all of the analytical requirements, such as having defined marker compounds for Other Extracts, may be appropriate.

The identity tests in the new EP include macroscopic, thin-layer chromatography (TLC), and microscopic, alongside new tests for aflatoxins, ochratoxin, residual solvents, heavy metals, and aristolochic acid. Colorimetric assays have been changed to liquid chromatographic (LC) methods.

In considering the future of TCM herbal drugs in the EP, Dr. Franz categorized them as single chemicals, complex mixtures, and Traditional Herbal Medicine as clinically used. He closed by noting that global collaboration is needed between the European Union (EU) and interested countries in order to make continued progress on harmonized monograph development.

Wolfgang Blaschek, PhD, from the Institute of Pharmacy in the Department of Pharmaceutical Biology at the University of Kiel in Kiel, Germany, followed with a talk titled “Herbal Medicinal Products: Regulatory guidelines for Efficacy and Safety in Europe.”

He discussed the European situation regarding all medicinal products, including Herbal Medicinal Products and the criteria for their marketing authorization of quality, safety, and efficacy in order to assess their risk-benefit analysis.

Dr. Blaschek explained that the European Medicines Agency (EMA) is a decentralized agency of the EU responsible for the scientific evaluation of medicines. Its management consists of a member and an alternate from 27 member states, making up six committees, including one for Herbal Medicinal Products. He discussed marketing access and the requirements for applications that include full applications, bibliographic applications, and mixed applications. He also covered Traditional Herbal Medicinal Product (THMP) applications and simplified registrations for which plausible efficacy can be shown on the basis of bibliographic data.

He also discussed the present situation where THMPs legally on the market have had a 7-year grace period prior to their required registration at the end of April 2011. A mutual recognition procedure was discussed whereby applicants receiving marketing authorization in one member state could market that product in all member states. The aims and responsibilities of the Committee for Herbal Medicinal Products (HMPC) were introduced as was the Community List of herbal substances, preparations, and combinations for use in THMPs.

Dr. Blaschek stated that the HMPC monographs are comprised of harmonized scientific opinion and also explained the different requirements between Well Established Use applications and THMP ones. He said that the European Scientific Cooperative on Phytotherapy's *ESCOP Monographs*, created by an umbrella organization of national scientific phytotherapy associations, and the 116 WHO medicinal plant monographs may also be helpful to industry. He closed by reminding the audience that the risk from most herbal medicine products is relatively low compared to other drugs but that pharmacovigilance regarding their use is still important.

Rudolph Bauer, PhD, from the Karl-Franzens-

University Graz in Graz, Austria, speaking on "Chinese Herbal Medicine in Europe: Regulatory Situation and Scientific Evaluation," discussed the determinations of these products as medicinal products or dietary supplements regarding applications using the EU regulatory framework. In the EU, food supplements are intended for health purposes providing a nutritional or physiological effect. Claims must be substantiated by studies and, like in the US, only health claims, and not disease claims, are allowed. With regard to novel foods and novel food ingredients, Dr. Bauer used the example of *Gynostemma pentaphyllum* (jiaogulan) in Germany, where it is considered as a novel food and sold as a type of tea.

Dr. Bauer also defined herbal medicine products as used for treating or preventing disease and THMPs as having limited applications, along the lines of those for over-the-counter drugs, and requiring a minimum of 30 years of use, of which 15 years must be in the EU. He also discussed challenges in the quality control of Chinese herbal preparations that include substitutions and adulterations, mixtures containing a high number of different herbs, the difficulty of obtaining authentic samples, and the fact that therapeutically relevant compounds in the herbs are often unknown. On top of that, the influence of different processing methods is not well known, and reference compounds are often lacking, all of which indicate the need for more research!

Dr. Bauer discussed the European prohibition of aristolochic acid-containing herbs and that the EP has TLC and high performance-liquid chromatography (HPLC) tests for aristolochic acid in herbal drugs. He mentioned the limit for external exposure of pyrrolizidine alkaloids of 100 mcg/day and the internal one at not more than 1 mcg/day. With regard to commonly used angelica species, he mentioned that TLC can differentiate them and that the spread of Chinese traditional herb use and herb preparation is now global. In a response to a question about Indian herbs, Dr. Bauer mentioned that there is a strong focus on herbal quality, safety, and efficacy in India but, unlike China, India does not have observer status at the European Pharmacopoeia Commission. He stated that in Europe overall herbal medicine is being discussed much more and that there is a higher acceptance of herbal medicines now than in recent years.



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Chinese Input

On Tuesday morning, De-An Guo, PhD, of the Shanghai Institute of Materia Medica in Shanghai, China, spoke generally about Chinese herbal medicine, describing how formulation strategy begins with yin and yang considerations and employs herbs in combination by their assignment to different roles represented by emperor, minister, assistant, and servant positions. He stated that this approach began empirically from examining a patient's face, taking their pulse, making a diagnosis, and then providing a formula. The medical theory now underpinning it was developed later to include about 12,000 herbs, of which 500-600 are commonly used.

In quantifying the commitment to Chinese medicine by the Chinese government, Dr. Guo said that about \$333 million has been committed and that this number will soon practically double. The Chinese Ministry of Scientific Technology and its National Science Foundation are involved in this effort. He reported that a delegation of 15 Chinese were in attendance at the conference. Dr. Guo discussed the Chinese Pharmacopoeia (CP), reporting that of the three volumes published every five years, the first volume is devoted to TCM. The 2010 CP edition provides multiple means to control quality, as assessing single marker compounds cannot do it.

Dr. Guo explained that Chinese regulations are very difficult to comply with and separate products into pure compounds, herbal fractions, and herbal mixtures. He added that the Chinese herbal products industry is making great strides with more than 1,000 TCM manufacturers, the biggest of which may have sales up to \$1 billion a year. Most are small manufacturers that may disappear or merge with other companies in order to survive in the face of new regulations that focus on quality standards and new drug approvals. He closed by announcing the 2011 International Conference on TCM Pharmaceutical Analysis, to be held July 1-3, 2011, in Chengdu, China. The theme of the event is "Standardization and Globalization of TCM."

Ling-Yi Kong, PhD, of the China Pharmaceutical University in Nanjing, China, presented a talk titled "Cytotoxic Triterpenoid Constituents from Two Plants

of Family Meliaceae" that focused on the application of LC and mass spectrometry (MS) methods in the isolation and structure identification of plant secondary metabolites. He was followed by Dao-Feng Chen, PhD, of the Fudan University in Shanghai, China, who spoke on "Isolation and Characterization of Anti-complementary Agents from Medicinal Plants." During questioning, it was pointed out that there are significant amounts of money spent in China on botanical research, but so far the work of the different research institutes isn't coordinated.

Improved Curcumin Absorption

Stefano Togni, PhD, from Indena S.p.A. in Milano, Italy, presented a talk titled "Development and Clinical Validation of Meriva[®], a Lecithin-Based Formulation of Curcumin" that is also the subject of a literature citation in this *AHPA Report*. On average, the phospholipid combination provided a 30-times increase in curcuminoid-plasma concentrations but a 60-fold increase in demethoxycurcumin, which may be a more potent anti-inflammatory compound than pure curcumin. Dr. Togni also discussed two osteoarthritis studies using this material, one of which involved 100 patients over 8 months taking a gram per day dosage.

US Concerns

The later morning session saw Mark Blumenthal of the American Botanical Council speaking on "Quality Control and Economically Motivated Adulteration of Botanical Raw Materials, Herbal Extracts, and Essential Oils in the Global Marketplace," in which he discussed the issue of purposeful adulteration. He credited the American Herbal Products Association's (AHPA) work in this area. He mentioned issues with solvent residues, and adulteration concerns with grapefruit seed extract, goldenseal, bilberry, black cohosh, ginkgo, pomegranate, and saw palmetto oil.

Loren Israelsen, executive director of the United Natural Products Alliance, provided a talk titled "A 20-Year Retrospective on the Progress of Botanical Supplement Regulation in the United States." In this talk, Israelsen supplied a brief history of supplement regulations, the rise in negative media, the appearance of cheap products, Chinese products, doping, social media, online healthcare communities, such as www.

patientslikeme.com and www.dailystrength.org, the *New England Journal of Medicine* article titled “American Roulette – Contaminated Dietary Supplements,” quality logo mania, new or old dietary ingredients, little botanical drug progress, limited healthcare and professional acceptance, botanical identity confirmation, and FDA funding and enforcement capability. It was, of course, both cogent and entertaining.

California District Attorney

In the Tuesday afternoon session on “Regulatory Aspects of Botanicals,” Daryl Roberts, JD, of the Napa County District Attorney’s Office in California, gave a talk titled “Regulation of Dietary Supplements: A Local Law Enforcement Perspective.” He spoke about the review for claims substantiation, stating that the Dietary Supplement Health and Education Act (DSHEA) did not define the level of evidence required in making claims. He also pointed out the difference between the Sherman Antitrust Act and California Proposition 65 by explaining the latter as a right-to-know statute that doesn’t protect customers from acute risks to health and safety, which is the job of the former. Rick Kingston, PharmD, of SafetyCall International PLLC in Bloomington, Minn., then presented “Are Botanicals Safer after Passage of Regulations for Mandatory Adverse Event Reporting in the US?” He raised the question of safety as being relative and provided a review of the calls received by his organization.

Indian Medicinal Plant Use

Ranjit Puranik from Shree Dhootapapeshwar Ltd. of Mumbai, India, gave a talk titled “Medicinal Plant Consumption in India: Reading the Data,” covering the developments of the last 10 years with a focus on the growth of the scope of the National Medicinal Plants Board (NMPB). He stated that there are 500,000 acres under conservation and an equal amount for contract cultivation under NMPB projects with mass scale “Mission Mode” programs for endangered medicinal plants. He presented the NMPB vision statement of herbs as sustainably sourced from organically certified forests and farms, with documentation supporting traceability and legal procurement, in full compliance with fair trade guidelines.

Puranik discussed a survey of 600 manufacturers

regarding herbal use. He reported that a total of 752 species were considered, resulting in a total herbal consumption of 80,000 tons, from which 397 species account for less than 10 tons. Only 10 species were reported as listed under the *Convention on International Trade in Endangered Species* (CITES). He provided two examples of reported harvests, namely 19 kgs of *Euphorbia neriifolia* (milk spurge or snuhi) and 71 tons of *Nardostachys jatamansi* (jatamansi) under cultivation. He also reported that the biggest users of these plants are not traditional medicinal plants manufacturers, but rather, large-scale exporters of raw materials, extracts, and phytochemical molecules. There is no tracking of this tonnage that involves 9,000 manufacturers, he said.

Puranik discussed that the average manufacturer may use over 100 species, and he spoke of the need to employ good agricultural and field collections practices. He also spoke about states’ organizations and joint forest-management committees that are trusts and societies of all forest tribal communities, whereby trade of what he called “forest produce” would be only through community trusts. He emphasized the need to attend to the use of certified species, and the importance of quality medicinal plant resources, chain of custody, and proper labeling practices. In closing, he mentioned the need to develop input-output ratios for wild collections that take into account the plant’s natural regeneration cycle.

US: Expert Panel, NCCAM, Research, Whole Herbs, and Analysis

Following a break, a panel discussion chaired by John Cardellina II, PhD, from the Office of Dietary Supplements at the National Institutes of Health, with Blumenthal; Israelsen; Duffy MacKay, ND, VP, Scientific & Regulatory Affairs for the Council of Responsible Nutrition; and me as panelists, fielded a wide range of questions from the audience.

Josephine Briggs, MD, director of the National Center for Complementary and Alternative Medicine (NCCAM), kicked off Wednesday’s program with a talk titled “Natural Product Research at NCCAM: Current Priorities.” She referenced NCCAM’s legislative mandate to support basic and applied research and the integration

of alternative treatment, and noted that about half of NCCAM's \$128 million annual budget funds such research. She discussed the lessons learned from previous trials, including where doubts have persisted regarding the efficacy of St. John's wort, echinacea, and ginkgo, and covered the promise of turmeric as an anti-inflammatory agent in light of a recent article published in the [British Medical Journal](#) that showed an increased cardiovascular risk from the use of nonsteroidal anti-inflammatory drugs.

Briggs emphasized that definitive testing of the efficacy of natural products and finding answers on their safety requires expertise in pharmacology and pharmacognosy. Birgit M. Dietz, PhD, from the University of Illinois-Chicago in Chicago, next spoke on "Cancer Preventive Properties of Botanical Dietary Supplements used in Women's Health with an Example of Hops and Black Cohosh," followed by Dennis B. Lubahn, PhD, of the University of Missouri-Columbia in Columbia, Mo., who discussed "What's New from the 'Elderberry Center,' also Called the Missouri University Center for Botanical Interaction Studies." Dr. Lubahn's botanical research center has again received 5-year funding after a 5-year hiatus. He spoke on a range of topics, including investigations regarding picrorhiza (*Picrorhiza kurroa*) for potential use for strokes as well as studies on soy, garlic, and elderberry with regard to prostate cancer, strokes, and immune system effects while attending to sourcing, identification, chemical analysis, transgenic animal models, and signaling systems studies.

Floyd "Ski" Chilton, PhD, of the Wake Forest Center in Winston-Salem, N.C., presented an interesting talk titled "Impact of Common Variants in Genes that Synthesize/Metabolize Fatty Acids on Levels of Inflammatory Fatty Acids in Subjects of African and European Ancestry," where he showed clear significant genetic variations of polyunsaturated fatty acid metabolism in human populations. Bill Helferich, PhD, from the University of Illinois at Urbana-Champaign, followed with a talk titled "Botanical Estrogens: Mechanism, Dose, and Target Tissues," where he suggested that isoflavones and equol may increase breast cancer metastasis from bone to lung.

Wendy Applequist, PhD, of the Missouri Botanical

Garden in St. Louis, spoke Thursday morning on "Morphological Assessment of the Identity of Selected Unprocessed Botanicals in Commerce." She began by emphasizing that the potential for adulteration or confusion between plants is plant (taxon) specific and related finding a recent lot of skullcap (*Scutellaria lateriflora*) herb that contained germander (*Teucrium chamaedrys*) herb. Applequist explained the material chain of custody and said that, generally speaking, wildcrafters and farmers see the whole material and pass it on to wholesalers and processors, who provide ingredients to manufacturers.

Dr. Applequist explained that herbs sold in the whole form that end up in herb shops are a minority of botanical materials sold. Whole herbs purchased this way are inexpensive and allow users to make their own custom formulas. Additionally, some herbs are not available as finished supplements and buying them whole may help avoid some types of adulteration. She asked the question, "Is the substitution of botanicals by incorrect species a problem for unprocessed herbs on the retail market?" and then presented the results of a project where herbs sold in whole or broken forms were intentionally selected to maximize observed adulteration. Herbs were ordered from retailers selected across the US by focusing on those subject to adulteration either by substitution of the wrong species or ones where unofficial related species were also used, namely skullcap, star anise, chamomile (sometimes adulterated with related genera with higher allergenic potential), St. John's wort, schisandra, juniper, linden (sometimes adulterated with unofficial species), arnica, hawthorn (species are used interchangeably), and chaste tree (can include related species).

Applequist found that some herbs were never adulterated while others almost always were, though toxic adulterants were not found. Juniper berry material was found to often contain fruit of other species in small amounts. Three schisandra samples had fruits of another species that may be used interchangeably in Chinese herbal medicine. Most samples of linden flower had other species mixed in and most of the arnica flower samples were not flowers of *Arnica montana* but instead most likely false arnica (*Heterotheca inuloides*) used in traditional Mexican herbal medicine. Applequist ended her talk by stating that most unprocessed herbs are

properly identified, though some species are suspect. She suggested that it would be interesting to see a chemical survey of commercial arnica products to determine what species were used as ingredients in the processed finished products.

Michael L. Eason, PhD, of the University of Texas at Austin in Austin, Texas, provided an interesting talk titled “Ex situ Plant Conservation in Texas and the Ethical and Sustainable Harvesting of Plant Material in the Southwest,” about his work with the Lady Bird Johnson Wildflower Center focusing on the access to and difficulties of plant collection. His talk was followed by one from Alain Touwaide, PhD, and Dssa Emanuela Appetiti, PhD., from the Institute for the Preservation of Medical Traditions in Washington, D.C., titled “Old Herbs New Remedies; Toward a New Paradigm,” discussing the challenges of gleaning herbal information from 800 BC – 1650 AD by reading ancient books. In order to be useful, texts must be available electronically, and the information contained within meaningfully organized. The linguistic problems with this work were discussed as well as the importance for the organized

information to be standardized and verifiable.

Amy Eichner, PhD, from the US Anti-Doping Agency in Colorado Springs, Colo., gave a talk titled “The Athlete’s Dilemma - Discerning Risk in Dietary Supplements,” during which she discussed the agency’s proposed launching of the Support of Online Resources and Tools (SORT) as a way to inform athletes about product quality and third-party testing. One suggestion she had for industry was for companies to consider sharing their FDA facility-audit results in a way that would be accessible to end-user customers.

John Travis, PhD, of NSF International, discussed the safety of products from the standpoint of the potential presence of illegal products in a presentation titled “Contaminants and Adulterants: Techniques to Unmask the Culprits.” Within the realm of anabolic steroids, diuretics, drugs of abuse, and stimulants, he gave specific analytical examples of analyzing for each of these drug categories. He stated that so far, in the phosphodiesterase type 5 (PDE5) inhibitor class of drugs, 20 analogues of sildenafil have been reported and five each of vardenafil



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and tadalafil. Travis said he will be looking next to broad, non-targeted screening while facing the problem of hard-to-find reference compounds. He pointed out the analytical difficulty of finding what is not supposed to be in a product when you don't know what it is and the general problem of working with complex matrices.

Melissa Phillips, PhD, from the National Institute of Standards and Technology (NIST) in Gaithersburg, Md., spoke on "NIST Tools for Quality Assurance in Botanical Dietary Supplement Measurements" and explained the differences between standard or certified reference materials, which can be used for their certified value, reference value, and information value, and standard reference materials (SRMs) that can be used for equipment calibrations. The institute's matrix-based SRMs made from crops are processed and should not be used as calibrants. She also discussed NIST's Dietary Supplement Laboratory Quality Assurance Program that now has 60 participants that participated in its last exercise. The breakdown of participating labs is approximately one-third 3rd-party testing laboratories, one-third industry labs, and one-third government and other interests.

Once again the ICSB demonstrated great value for the range of content and quality of the talks, the networking opportunities, and overall significance for botanical science issues of interest to industry. The dates for next year's meeting are April 16-19, 2012. I suggest you mark your calendars now!

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Individual TCM Herbal Treatments Rigorously Tested

- ◆ Flower A, Lewith G, Little P. [Combining rigour with relevance: A novel methodology for testing Chinese herbal medicine.](#) *J Ethnopharmacol.* 2011 Mar 24;134(2):373-378.

The clinical practice of herbal medicine often involves the administration of individualized preparations. This is a drawback for conducting randomized, double-blind,

placebo-controlled clinical trials that are relevant to actual practice. This feasibility study provided either a placebo or an individualized Chinese herbal preparation to participants, thereby combining the practice of TCM with a rigorous clinical trial design.

Treating Chronic Disease with TCM

- ◆ Jiang M, Zhang C, Cao H, Chan K, Lu A. [The role of Chinese medicine in the treatment of chronic diseases in China.](#) *Planta Med.* 2011 Apr 6. doi:10.1055/s-0030-1270983 [Epub ahead of print]

Traditional Chinese medicine, which accounts for about 20 percent of Chinese health care, is seeing increasing use in treating chronic disease in China. This review examines its importance relative to the Western medical approach, evidence of its safety and efficacy, and approaches to patient classification and determining mechanisms of action of complex herbal mixtures with a view toward the integration of traditional Chinese medicine in health care worldwide.

Plant Aphrodisiacs Reviewed

- ◆ Melnyk JP, Marcone MF. [Aphrodisiacs from plant and animal sources—A review of current scientific literature.](#) *Food Res Int.* 2011 Mar 5. doi:10.1016/j.foodres.2011.02.043. [Epub ahead of print]

This review assessed the current scientific literature for evidence of the sexual-enhancing properties for several botanicals including Asian ginseng (*Panax ginseng*), "horny goat weed" (*Epimedium* spp.), maca (*Lepidium meyenii*), muira puama (*Ptychopetalum olacoides*), tribulus (*Tribulus terrestris*), yohimbine (an alkaloid from yohimbe, aka *Pausinystalia yohimbe*), and others including nutmeg, saffron, and chocolate (cacao). The authors conclude that the potential exists for many of these to be used as aphrodisiacs but that more research is needed to establish their function in humans, including clinical trials, before definitive conclusions about their effectiveness can be drawn.

Review of Phytochemical Databases

- ◆ Scalbert A, Andres-Lacueva C, Arita M, Kroon P, Manach C, Urpi-Sarda M, Wishart D. [Databases on food phytochemicals and](#)

[their health promoting effects](#). *J Agric Food Chem*. 2011 Mar 28. [Epub ahead of print]

The content and limits of over 50 phytochemical databases are reviewed in this article that discusses their utility and directions for future improvements.

New Philosophical Approach to Rationalizing Phytotherapy

- ◆ Gertsch J. [Botanical drugs, synergy, and network pharmacology: Forth and back to intelligent mixtures](#). *Planta Med*. 2011 Mar 16. [Epub ahead of print]

This thought-provoking mini-review starts off by reminding us that traditional pharmacognosy was reverse engineered to discover pharmacologically active molecules and leads for new drugs. It then asks if botanicals also provide effective mixtures, pointing out that sound experimental data are widely lacking to prove that whole herbs are better than purified chemicals extracted from them. The author suggests that the emerging concept of network pharmacology may be fundamental to understanding and rationalizing botanical use. His review is replete with discussions on mixtures, synergies, the dangers of drug interactions, and polypharmacy. He insists that the study of the pharmacodynamics of botanical drugs is necessary to rationalize phytomedicine use.

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Review of TCM Materials on Learning and Memory Impairment

- ◆ Jesky R, Hailong C. [Are herbal compounds the next frontier for alleviating learning and memory impairments? An integrative look at memory, dementia and the promising therapeutics of Traditional Chinese Medicines](#). *Phytother Res*. 2011 Feb 9. doi: 10.1002/ptr.3388. [Epub ahead of print]

This review provides an overview of memory and dementia with a focus on Alzheimer's disease processes before examining the effects on them of several Traditional Chinese Medicine botanical materials,

including compounds and extracts from ginseng (*Panax ginseng*), ginkgo (*Ginkgo biloba*), *Polygala tenuifolia*, Chinese smilax (*Smilax china*), bacopa (*Bacopa monnieri*), *Huperizia serrata*, and others.

Açaí on the Internet: Little Data for Claims

- ◆ Heinrich M, Dhanjia T, Casselmana I. [Açaí \(*Euterpe oleracea* Mart.\)—A phytochemical and pharmacological assessment of the species' health claims](#). *Phytochem Lett*. 2011 Mar 15;4(1):10-21.

This mini-review found limited evidence for açai health claims after reporting that Google searches for “açai” showed a dramatic increase in 2008–2009, peaking in mid-2009, with a subsequent drop off since. The authors speak to the “power of the Internet to promote products for which only limited phytochemical and pharmacological information is available.” They also review phytochemical and pharmacological research on this nutritious food material.

Quality of Herbal AER Case Reports

- ◆ Hung SK, Hillier S, Ernst E. [Case reports of adverse effects of herbal medicinal products \(HMPs\): A quality assessment](#). *Phytomedicine*. 2011 Mar 15;18(5):335-343.

This UK study reviewed the quality of literature reporting for Herbal Medicinal Product adverse-event case reports for three two-year periods over three decades. The authors found that reports have increased over time, though the quality of the reports suffers from similar deficits seen with reports for conventional medicine adverse events. The researchers also pointed out that their evaluation scale requires additional research to validate it and that the quality of case reporting of conventional medicines should also be looked into.

Moldy Kava to Blame for Liver Toxicity?

- ◆ Teschke R, Qiu SX, Lebot V. [Herbal hepatotoxicity by kava: Update on pipermethystine, flavokavain B, and mould hepatotoxins as primarily assumed culprits](#). *Dig Liver Dis*. 2011 Mar 7. doi:10.1016/j.dld.2011.01.018. [Epub ahead of print]

Coincident with the publication of a kava article by

Rolf Teschke, MD, in last month's *AHPA Report*, this report evaluates the evidence for kava toxicity caused by pipermethystine, flavokavain B, and mold hepatotoxins. Possible types of kava hepatotoxicity were examined, including in some cases the possibility of rare idiosyncratic reactions in particularly susceptible individuals. The authors conclude that there may be additional cases caused by mold hepatotoxins but that further studies are needed to evaluate this possibility.

Ionizing Irradiation for Phytosanitary Uses

- ◆ Hallman GJ. [Phytosanitary applications of irradiation](#). *Compr Rev Food Sci Food Saf* 2011 Mar;10(2):143-151.

This comprehensive review, available for free download, discusses the use of ionizing radiation to sanitize food, including fruits and vegetables that are sold in the US. Such use effectively sterilizes insects and leads to their death without the problem of residual pesticides. Such treatment is not acceptable under organic certification requirements. Other disadvantages are discussed with suggestions of how to deal with existing challenges for wider use of phytosanitary irradiation.

Strategies for Ingredient Validation by NIR

- ◆ Sileoni V, van den Berg F, Marconi O, Perretti G, Fantozzi P. [Internal and external validation strategies for the evaluation of long-term effects in NIR calibration models](#). *J Agric Food Chem*. 2011 Mar 9;59(5):1541-1547.

This article uses the example of brewing malt to demonstrate the long-term use of NIR calibrations and shows that NIR identification, done properly, is not a simple matter. I recommend any company that employs NIR identity testing, or is considering it, to consult this paper in order to get an idea of how chemometrics need to be employed in order for the NIR identity methods to be scientifically valid.

Heavy Metal Analysis of Herbal Materials

- ◆ Yuan X, Chapman RL, Wu Z. [Analytical methods for heavy metals in herbal medicines](#). *Phytochem Anal*. 2011 Feb 21. doi: 10.1002/pca.1287.

Analysis of botanical materials for heavy metals is routinely done by inductively coupled plasma-mass

spectrometry (ICP-MS). This review discusses this and several other commonly used and sensitive analytical techniques in detail and provides applied examples for analysis of herbal medicines. Less commonly used techniques are also discussed. This is a basic yet comprehensive review of methods of heavy metal analysis that have been used in testing herbal medicines with a description of how each method works and examples of its use in practice.

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Common Herbal Extracts Prevent Bacterial Adhesion

- ◆ Bensch K, Tiralongo J, Schmidt K, Matthias A, Bone KM, Lehmann R, Tiralongo E. [Investigations into the antiadhesive activity of herbal extracts against *Campylobacter jejuni*](#). *Phytother Res*. 2011 Jan 31. doi: 10.1002/ptr.3384. [Epub ahead of print]

Additional potential benefits from herbs in treating gastric disorders are reported in this third paper from *Phytotherapy Research* that looked at the anti-adhesion effects of 21 hydroethanol herbal extracts against *Campylobacter jejuni*, a common bacterial cause of diarrhea. It is thought that *C. jejuni* may exert its detrimental effects by first adhering to the walls of the intestines and then producing toxins. If this is true, a treatment that prevents adhesion may ward off the ill-effects of eating *C. jejuni*-contaminated food. Unlike the previous two studies, this one did not involve human or animal subjects; it involved only human colon cells in an anti-adhesion assay. The strongest inhibitors of bacterial binding to the human cells were licorice (*Glycyrrhiza glabra*), cayenne (*Capsicum annum*) and ginger (*Zingiber officinale*). Cytotoxic and antibacterial effects of the extracts were also determined.

Herbal Traditions in Bosnia and Herzegovina

- ◆ Sarić-Kundalić B, Dobeš C, Klatter-Asselmeyer V, Saukel J. [Ethnobotanical survey of traditionally used plants in human therapy of east, north and north-east](#)

[Bosnia and Herzegovina. J Ethnopharmacol.](#)
2011 Feb 16;133(3):1051-1076.

If you want to take advantage of the herbal knowledge of traditional healers it helps if that information is recorded. Someone has to ask those with the knowledge and then record it. This ethnobotanical survey of traditionally used plants of east, north and north-east Bosnia and Herzegovina complements an earlier one done for middle, southern and western Bosnia and Herzegovina. This time the identity, location, and indications for 254 plants used in 1,655 different preparations were gleaned from interviewing 84 people in 45 locations. The plants, preparation forms, and indications were compared with those of the earlier study. Knowledge was typically passed down from mother to daughter, and this had been done for over six generations in some cases.

Patented Essential Oils Used to Repel Mosquitoes

- ◆ Pohlit AM, Lopes NP, Gama RA, Tadei WP, de Andrade-Neto VF. [Patent literature on mosquito repellent inventions which](#)

[contain plant essential oils – A review.](#)
Planta Med. 2011 Feb 15. doi: 10.1055/s-0030-1270723. [Epub ahead of print]

Preventing mosquito bites can sometimes obviate the need to treat malaria. This review reported on a search of the literature from 1991 through May 2010 for patents involving essential oils and mosquito repellency and analyzed them according to which country they were from, what language is utilized, the essential oils mentioned, and what type of patents they represent. It also provides text and tables that include information on the essential oils, extraction methods, scientific evidence for mosquito repellency, and the repellency or deterrent effects of individual essential oil components used in the patent inventions. The authors point out that the best formulation results will likely be achieved by targeting local and regional mosquitoes for the repellent properties of the product.

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- ◆ [Papers from the 2010 DSHEA Symposium, Chicago, IL, USA, DSHEA 2010](#)

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Symposium Chicago. Edited by Pauli G. *Fitoterapia* 2011 Jan;82(1):1-92.

I reported on this symposium in the April 2010 *AHPA Report* (volume 25, number 4, pages 24-29) under the title, *Developments in Botanical Dietary Supplements Research 1994 to Today*. It was held to celebrate the 80th birthday of Norman Farnsworth, PhD, the guest of honor. The journal *Fitoterapia* has made the complete proceedings available. It was a remarkably well-rounded and informative symposium with the sessions now available for free download from the journal's [website](#).

Diet, Supplements, and Mental Energy:

A Review

- ◆ Gorby HE, Brownawell AM, Falk MC. [Do specific dietary constituents and supplements affect mental energy? Review of the evidence.](#) *Nutr Rev.* 2010 Dec;68(12):697-718.

The effects of ginkgo, ginseng, glucose, and omega-3 polyunsaturated fatty acids on the three aspects of mental energy identified as mood, motivation, and cognition are described in this review article written by the Life Sciences Research Organization (LSRO) of Bethesda, Md. This work evaluated the scientific literature through May of 2010, after the creation of a scientific definition of mental energy that followed a series of workshops hosted by the North American branch of the International Life Sciences Institute (ILSI).

The LSRO review contains tables of published studies of these four materials on mental energy and an analysis of those studies. Definite conclusions could not be drawn regarding ginkgo's effect on mood, and variable results were found from examination of the studies on cognition. Potential improvements on attention were suggested after short-term administration in young and old, and a positive effect on memory was suggested in several other studies, although on the whole the authors concluded that there is insufficient evidence to determine if ginkgo improves memory.

The research on ginseng (*Panax ginseng*) and glucose was also conflicted. The available evidence on omega-3 polyunsaturated fatty acids suggests the possibility of delaying or reducing cognitive decline in the elderly,

though more research is needed to determine when and how much of this material needs to be taken to impact cognitive decline and which types of tasks may be affected. The article concludes by pointing out the difficulties in evaluating the data in part due to the "immense variety of testing instruments," variations in trial design, and the need for relevant biomarkers that could be measured in future studies.

Herb, Drug, and Author Interactions

- ◆ Colalto C. [Herbal interactions on absorption of drugs: Mechanisms of action and clinical risk assessment.](#) *Pharmacol Res.* 2010 Sep;62(3):207-227.
- ◆ Vlachojannis J, Cameron M, Chrubasik S. [Drug interactions with St. John's wort products.](#) *Pharmacol Res.* 2011 Mar;63(3):254-256.
- ◆ Colalto C. [Response to the letter "Drug interactions with St. John's wort products".](#) *Pharmacol Res.* 2011 Mar;63(3):257-258.

The first citation is a review of how herbal materials may impact the absorption of drugs and what that may mean in clinical settings. It is interesting, fairly comprehensive, and concludes, among other things, that there is good documentation that St. John's wort (*Hypericum perforatum*), grapefruit juice, black pepper, and fiber may cause herb-drug interactions. Its publication provoked a letter to the editor (the second citation) that presents a very good description of the evidence for St. John's wort-drug interactions to date, complete with an extensive table. This provided the author of the original article with the opportunity to reply in a way some readers might consider as snippy.

However, in discussing how pharmacologists can contribute to the safety and efficacy of herbal products in a way that translates to best clinical practices, Dr. Colalto invoked a mnemonic from another article (Glisson JK, Walker LA. [How physicians should evaluate dietary supplements.](#) *Am J Med* 2010 May 20;123:577-582) known as CARE where "the authors proposed the following challenges: a 'free' but attentive [C]ommunication with the patients in a 'non-confrontational manner,' [A]cquiring knowledge and reference about supplements, becoming a [R]eporter of adverse events and managing possible

interactions, examining and [E]valuating literature objectively.”

A more complete review of the original article is below. The review was written by Francis Brinker, ND, author of *Herbal Contraindications and Drug Interactions plus Herbal Adjuncts with Medicines, Fourth Edition* (2010 Eclectic Medical Publications, Sandy, Ore.).

Overall, the coverage of drug-herb interactions in this review article is thorough and relatively balanced, but it becomes typically cloudy in addressing some important differences in studying botanicals in comparison to pharmaceutical isolates. The author extensively discusses *in vitro* studies that do not represent systemic exposure to the phytochemical content of complex extracts, which is how herbal preparations most influence function in humans. However, the examination of the *in vitro* studies in this review may be more appropriate as it is associated with the author’s emphasis on drug absorption that involves localized exposure to intestinal transporters and metabolic enzymes, in contrast to post-absorption effects on the liver. Nonetheless, there have commonly been inconsistencies between findings from *in vitro*, animal, and/or human drug studies of metabolizing enzymes (cytochrome P-450 or CYP) for herbs and herbal extracts in these different contexts. To his credit, Dr. Colalto primarily limits his conclusions for each herb to higher-quality evidence from human study outcomes.

The other failure of the review in botanical terms was an inadequate analysis of particular phytochemical differences in distinctive preparations of the same herb that can result in conflicting data. The author attributes various contrasting human results from some herbal preparations to genetic polymorphisms, which would be due to differences in individual humans. While genetically determined differences in how humans react to drugs (pharmacogenetics) are an important aspect of variations in human response to herbs, so is the phytochemical variability between different herbal preparations. Aside from noting the example of differing outcomes obtained from high-hyperforin vs. low-hyperforin St. John’s wort preparations, the author inappropriately suggested that a 12-week study with 52 patients “failed to confirm a garlic-warfarin interaction”

when in fact that study utilized an aged garlic extract (stated explicitly in the title of the article) which is distinctively different in content and CYP impact from fresh garlic or garlic oil.

Checking *Echinacea* species (spp.) discussions is often a good indicator as to whether the author knows about important differences between products. This author did occasionally specify *E. purpurea* and once acknowledges use of its root extract, but states of *Echinacea* spp. in general: “The extract consists mainly of lipophilic constituent alkaloids with immunomodulatory properties.” That generalization may be about half accurate in regard to roots, but when addressing *E. purpurea* aerial or whole-plant extracts it is mostly wrong, and does not apply to *E. pallida* root products at all. Sure enough, when quoting negligible CYP results from the whole-plant extract that conflict with root-extract positive findings, the author fails to make the connection, even though the Gurley et al. 2004 article he cites points this out in the discussion section of that article.

The attempts to treat herbs like single-compound drugs will continue to be a problem for those who fail to acknowledge the fact that the inherent variability in content is part of the challenge in the interpretation of botanical data that reviewers must learn to discern. The desire to impose drug standards on herbal preparations will inevitably be achieved for a few pharmaceutically manufactured botanical products with standardized conformity and significantly reduced complexity. The rest of the herbal marketplace may be subjected to attempts to harness or suppress traditional and innovative processes, but since herbs grow in variable soils and are processed in many acceptable but differing ways, ultimately well-intentioned but misinformed attempts to constrain the spectrum of effective herbal preparations will fail.

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verify the identity of each of the herbal ingredients they use.

“This text is an essential reference for herbal manufacturers at this time of increased cGMP scrutiny,” says Michael McGuffin, president of the American Herbal Products Association (AHPA). “For companies that purchase herbal ingredients, especially in powdered form, microscopy may be the most affordable tool for meeting their cGMP identity verification requirement.” McGuffin has served as a volunteer board member of AHP for many years.

The AHP microscopy text is now available to IASC members at a 10 percent discount from its retail cost of \$169.95. To order, [contact AHP](#).

“The work of AHP is solely based on creating a strong foundation of quality control for the herbal products market and provides direct benefit to all of IASC’s members,” notes Roy Upton, executive director of AHP and the lead editor of the new microscopy text. “The genesis of this work arose from discussions in AHPA’s Standards Committee meetings and would not have materialized without the efforts of AHPA President Michael McGuffin, who secured partial funding for it through ODS. In this regard, this text is the shared work of AHP and AHPA and is a testimony of what we can accomplish when working collaboratively.” To learn more about the microscopic identification of botanicals, AHPA is offering a 2-day, hands-on, educational training to assist both manufacturers and suppliers in establishing identity. The AHPA seminar, [Microscopic Identification of Popular Botanical Materials](#), to be held in the fall of 2011, provides participants the experience necessary to conduct microscopic analysis on a variety of popular botanical ingredients.

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LEGAL & LEGISLATIVE NEWS

A Look Back Provides a Glimpse of Legislative Action to Come

By Peter Evich, National Legislative Consultant, Van Scoyoc Associates.

The 112th Congress is now in full-operation mode. Congressional committee assignments have been finalized in both the House and Senate and legislative workings such as hearings, debate, and votes have begun in earnest.

The Recent Past as Prologue?

In an attempt to determine what may be in store on the legislative front for the supplement industry in 2011, one barometer is to examine some of the key bills from the 111th Congress that *would have* impacted this trade, but were not enacted. Here are five such “leftover” measures, along with a brief explanation of each:

- ◆ *The Food Safety Accountability Act (S.3767)*: Introduced by Sen. Patrick Leahy, D-VT, chairman of the Senate Judiciary Committee, this bill would have increased the sentences that prosecutors can seek, to up to ten years imprisonment for food-safety violations where there is a conscious or reckless disregard of a risk of death or serious bodily injury. Last year, Sen. Orrin Hatch, R-UT, worked with Leahy to eliminate a section of the bill that tied these enhanced penalties to violations surrounding new dietary ingredient (NDI) applications. Leahy has reintroduced this legislation (not applicable to NDIs) on January 27 as S.216.
- ◆ *Dietary Supplement Safety Act of 2010 (S.3002)*: Introduced by Sen. John McCain, R-AZ, this legislation would have placed several onerous regulations and requirements on dietary supplements. For more information on this legislation, click [here](#) to see the *AHPA Update* of February 3, 2010.
- ◆ *Dietary Supplement Full Implementation and Enforcement Act (S.3414 and H.R.3236)*: Introduced in the Senate by Sens. Hatch and

and Government Reform Committee, Rep. Darrell Issa, R-CA, will be holding several hearings in the coming months on how federal regulatory agencies have been working with stakeholders and the entities that they are charged with regulating. We will also see similar hearings conducted by the House Energy and Commerce Committee's Oversight and Investigations Subcommittee.

Time for a Non-Defensive Posture?

As I indicated in my last *AHPA Report* article (see the [January 2011 AHPA Report](#)), due to the Republican takeover of the lower chamber, the House leadership and committee power brokers have changed from the last Congress. Reps. Henry Waxman, D-CA, and John Dingell, D-MI, who have been formidable critics of supplements, are no longer controlling the policy strings at the House Energy and Commerce Committee. And the Senate is once again on firm terrain, with Harkin as the chairman of HELP, along with Hatch as ranking member of Senate Finance—in addition to also having a seat on Senate HELP.

These developments do not mean we can or should lower our guard. We know from the past that it only takes one or two high-profile news articles to lead to congressional scrutiny, which will be accompanied by misplaced calls to add further regulatory burdens to the supplement industry. Therefore, we can never succumb

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to complacency and we will maintain our vigilance. Conversely, though, the situation at hand may present a unique opportunity for the supplement community to—for the very first time—take an offensive posture as it relates to public policy. For example, is it time to consider advancing a DSHEA-type statutory framework for animal supplements?

The 112th Congress has resulted in several new faces on the congressional committees that are key to our trade, such as policy jurisdiction and oversight for FDA, the Federal Trade Commission (FTC), and the U.S. Department of Agriculture (USDA), as well as 96 recently inaugurated members of the House and 16 new senators.

With that as a backdrop, AHPA President Michael McGuffin and I have begun to meet with congressional offices to educate members and staff about the herbal supplement trade, the strong federal regulatory structure that currently governs this industry, and our current collaborations with federal agencies. As always, we value and welcome your input related to AHPA's federal advocacy efforts. We ask that you let us know if there are topics of particular interest to you and look forward to being your advocates during our congressional visits.

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THE SCIENCE OF ALOE RECENTLY PUBLISHED STUDIES

[Antimicrobial efficacy of oral topical agents on microorganisms associated with radiated head and neck cancer patients: an in vitro study](#)

Abstract

Objective: A variety of oral topical agents have been used for prevention and management of radiotherapy-induced adverse effects. The antimicrobial nature of some of the commonly used agents is unknown. The purpose of this study was to evaluate antimicrobial efficacies of various oral topical agents on common microorganisms associated with radiated head and neck cancer patients. Method and Materials:

Seven commonly used topical oral agents-0.12% chlorhexidine with alcohol, 0.12% chlorhexidine without alcohol, baking soda-salt rinse, 0.4% stannous fluoride gel, 0.63% stannous fluoride rinse, calcium phosphate mouthrinse, and acemannan hydrogel (aloe vera) rinse-were evaluated in vitro for their antimicrobial efficacies against four common microorganisms. A combination of baking soda-salt rinse and 0.4% stannous fluoride gel was evaluated as the eighth agent. The microorganisms used were *Staphylococcus aureus*, group B *Streptococcus*, *Escherichia coli*, and *Candida albicans*. An ELISA reader was used to measure the turbidity of microbial culture wells and optical density (OD) values for each of the 960 wells recorded. Mean OD values were rank ordered based on their turbidity. One-way ANOVA with Tukey HSD post hoc analysis was used to study differences in OD values ($P < .05$). Results: Mean OD values classified for topical agents from lowest to highest were chlorhexidine with alcohol, chlorhexidine without alcohol, baking soda- salt, calcium phosphate rinse, and the combination of baking soda-salt and stannous fluoride gel. Mean OD values classified for microorganisms from lowest to highest were *Escherichia coli*, *Staphylococcus aureus*, group B *Streptococcus*, and *Candida albicans*. Conclusion: A significant difference among the antimicrobial efficacies of topical agents was evident for each of four microorganisms ($P < .05$). There was also a significant difference among the antimicrobial efficacies of the same topical agent on the four microorganisms tested ($P < .05$). (Quintessence Int 2011;42:307-315).

Plants used for treating respiratory infections in rural Maputaland, KwaZulu-Natal, South Africa

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE:

Traditional remedies are frequently used in treating various respiratory ailments, and are very important in the primary health care of the people living in rural Maputaland, KwaZulu-Natal, South Africa. Novel information gathered from surveys like the present study is important in preserving indigenous knowledge.

AIM OF THE STUDY:

To explore the knowledge that the lay people of a rural community in northern Maputaland have about medicinal plants used in the vicinity to treat respiratory infections.

MATERIALS AND METHODS:

Interviews were conducted among 80 homestead inhabitants, using structured questionnaires where convenience sampling was used. The focus was on plants used in treating respiratory infections. Some of the main topics discussed during the interviews were vernacular plant names, plant parts used, harvested amounts, preparation methods, dosage forms and quantities, use of plants in combination as well as the related symptomatic relief associated with respiratory infections.

RESULTS:

The study documented 30 plant species (18 families) which are used to treat respiratory infections by the rural people in the study area. Decoctions made with these plants are mostly taken orally, combined with the use of steaming. To the best of our knowledge, *Acanthospermum glabratum*, *Aloe marlothii*, *Krauseola mosambicina*, *Ozoroa obovata*, *Parinari capensis* and *Plectranthus neochilus* are recorded for the first time globally as medicinal plants used for treating respiratory infections and related symptoms. The indigenous aromatic shrub, *Lippia javanica* was by far the most frequently used plant species, followed by *Eucalyptus grandis* (an exotic), *Tetradenia riparia* and then *Senecio serratuloides*. Twenty-four different plant combinations were used where the most frequently used combination encountered was *Eucalyptus grandis* with *Lippia javanica*.

CONCLUSION:

The large number of different plant species traditionally used against respiratory infections supports previous research on the importance of traditional medicine in the primary health care of this remote area. The finding of new vernacular plant names and plant uses in the current survey shows the importance of the documentation of such ethnobotanical knowledge.

Dietary aloe improves insulin sensitivity via the suppression of obesity-induced inflammation in obese mice

Abstract

BACKGROUND:

Insulin resistance is an integral feature of metabolic syndromes, including obesity, hyperglycemia, and hyperlipidemia. In this study, we evaluated whether the aloe component could reduce obesity-induced inflammation and the occurrence of metabolic disorders such as blood glucose and insulin resistance.

METHODS:

Male C57BL/6 obese mice fed a high-fat diet for 54 days received a supplement of aloe formula (PAG, ALS, Aloe QDM, and Aloe QDM complex) or pioglitazone (PGZ) and were compared with unsupplemented controls (high-fat diet; HFD) or mice fed a regular diet (RD). RT-PCR and western blot analysis were used to quantify the expression of obesity-induced inflammation.

RESULTS:

Aloe QDM lowered fasting blood glucose and plasma insulin compared with HFD. Obesity-induced inflammatory cytokine (IL-1 β , -6, -12, TNF- α) and chemokine (CX3CL1, CCL5) mRNA and protein were decreased markedly, as was macrophage infiltration and hepatic triglycerides by Aloe QDM. At the same time, Aloe QDM decreased the mRNA and protein of PPAR γ /LXR α and 11 β -HSD1 both in the liver and WAT.

CONCLUSION:

Dietary aloe formula reduces obesity-induced glucose tolerance not only by suppressing inflammatory responses but also by inducing anti-inflammatory cytokines in the WAT and liver, both of which are important peripheral tissues affecting insulin resistance. The effect of Aloe QDM complex in the WAT and liver are related to its dual action on PPAR γ and 11 β -HSD1 expression and its use as a nutritional intervention against T2D and obesity-related inflammation is suggested.

Aloe vera oral administration accelerates acute radiation-delayed wound healing by stimulating transforming growth factor- β and fibroblast growth factor production

Abstract

BACKGROUND:

Delayed wound healing is a significant clinical problem in patients who have had previous irradiation. This study investigated the effectiveness of Aloe vera (Av) on acute radiation-delayed wound healing.

METHODS:

The effect of Av was studied in radiation-exposed rats compared with radiation-only and control rats. Skin wounds were excised on the back of rats after 3 days of local radiation. Wound size was measured on days 0, 3, 6, 9, and 12 after wounding. Wound tissues were examined histologically and the expressions of transforming growth factor β -1 (TGF- β -1) and basic fibroblast growth factor (bFGF) were examined by immunohistochemistry and reverse-transcription polymerase chain reaction.

RESULTS:

Wound contraction was accelerated significantly by Av on days 6 and 12 after wounding. Furthermore, the inflammatory cell infiltration, fibroblast proliferation, collagen deposition, angiogenesis, and the expression levels of TGF- β -1 and bFGF were significantly higher in the radiation plus Av group compared with the radiation-only group.

CONCLUSIONS:

These data showed the potential application of Av to improve the acute radiation-delayed wound healing by increasing TGF- β -1 and bFGF production.

Effect of Aloe vera gel extract on antioxidant enzymes and azoxymethane-induced oxidative stress in rats

Abstract

The present work was undertaken with a view to study the effect of oral feeding of 2% Aloe vera gel extract (AGE) for 30 days on azoxymethane (AOM)-induced oxidative stress in rats. It was observed that AOM administration resulted in a significant increase

in malondialdehyde and conjugated dienes, with reduction in hepatic glutathione (GSH), vitamin A and uric acid contents. AOM-induced reduction in hepatic GSH and uric acid was brought back to normal by AGE. There was a significant raise in hepatic catalase, superoxide dismutase and glucose-6-phosphate dehydrogenase (G-6-PD) activities as a result of feeding of the extract. Ingestion of the extract effected reduction in AOM-induced colonic GSH-oxidase, G-6-PD and glutathione S-transferase and femur bone marrow micronuclei formation. Hence, it is suggested that Aloe vera gel extract possess the ability to reduce AOM- induced oxidative stress and toxicity in liver.

Circadian variations in biologically closed electrochemical circuits in Aloe vera and Mimosa pudica

Abstract

The circadian clock regulates a wide range of electrophysiological and developmental processes in plants. This paper presents, for the first time, the direct influence of a circadian clock on biologically closed electrochemical circuits in vivo. Here we show circadian variation of the plant responses to electrical stimulation. The biologically closed electrochemical circuits in the leaves of Aloe vera and Mimosa pudica, which regulate their physiology, were analyzed using the charge stimulation method. The electrostimulation was provided with different timing and different voltages. Resistance between Ag/AgCl electrodes in the leaf of Aloe vera was higher during the day than at night. Discharge of the capacitor in Aloe vera at night was faster than during the day. Discharge of the capacitor in a pulvinus of Mimosa pudica was faster during the day. The biologically closed electrical circuits with voltage gated ion channels in Mimosa pudica are also activated the next day, even in the darkness. These results show that the circadian clock can be maintained endogenously and has electrochemical oscillators, which can activate ion channels in biologically closed electrochemical circuits. We present the equivalent electrical circuits in both plants and their circadian variation to explain the experimental data.

Skin tolerability of transdermal patches

Abstract

Introduction: Transdermal patch systems are an effective method of administering active ingredients through the skin, with considerable advantages over other drug delivery routes, for example, maintenance of constant plasma drug levels and avoidance of first-pass metabolism. However, repeated epicutaneous application may be associated with local skin reactions. **Areas covered:** This review addresses current issues regarding the effective/safe use of transdermal patch systems, and provides a critical analysis of the addition of 'skin-caring' ingredients to patch systems. Effective use of transdermal systems includes choosing an appropriate body area for application, maintaining regular skin care regimens before application and not replacing a patch in the same area (rotation) within 7 days. Another strategy, developed in an attempt to improve the tolerability of transdermal systems, is the addition of assumed 'skin-caring' ingredients (e.g., Aloe Vera) to patch systems. However, at present there is neither proof nor clinical evidence of any benefit. On the contrary, plant-derived ingredients might be associated with allergenic potential. **Expert opinion:** Transdermal systems are generally well tolerated; physicians must adequately inform patients of the most effective ways to use these formulations for maximum therapeutic benefit, while minimising local adverse events. Skin-caring agents, including Aloe Vera, cannot be recommended until well-controlled clinical trials with standardised extracts are available.



REGULATORY NEWS

FDA Issues Import Alert for Japanese Products and Consumer Radiation Notice

The Food and Drug Administration (FDA) announced that it is automatically flagging all shipments of FDA-regulated products imported from Japan and has issued an [Import Alert](#) regarding the importation of all milk products and fresh produce from the four Japanese prefectures of Fukushima, Ibaraki, Tochigi and Gunma.

Entry of such products—which the agency acknowledges to be quite limited at this time—will be allowed only if shown to be free from radionuclide contamination, and other food products from Japan, such as seafood, will be diverted for testing by FDA before they can enter the US food supply.

“FDA advises consumers “ ... to be wary of internet sites and other retail outlets promoting products making false claims to prevent or treat effects of radiation or products that are not FDA-approved.”

The agency’s Import Alert specifies “detention without physical examination of products from Japan due to radionuclide contamination.” It adds an Internet link to FDA’s [methodology](#) used in radionuclide analysis and provides background for its actions. The alert also expands the products included in a list of those restricted for export by the Government of Japan.

Additionally, FDA has issued a [Public Health Focus](#), titled “Radiation Safety,” that answers questions about the threat of radiation, provides guidance on medicines and other products for use as an adjunct to other public health protective measures “in the event that radioactive iodine is released into the environment,” and outlines what the U.S. government is doing to protect public health. In this document, FDA states that “the U.S. Government is not recommending that residents of the United States or its territories take KI (potassium iodide), even as a preventative measure.”

Also of note, FDA advises consumers “ ... to be wary of internet sites and other retail outlets promoting products making false claims to prevent or treat effects of radiation or products that are not FDA-approved. These fraudulent products come in all varieties and

could include dietary supplements, food items, or products purporting to be drugs, devices or vaccines.”

For more information, contact [Michael McGuffin](#), AHPA president.

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FDA Holds Meetings on Import Provisions of New Food Safety Law

By Merle Zimmermann, AHPA Information Analyst.

The Food and Drug Administration (FDA) held public meetings on March 29 and March 30-31 on how FDA should implement certain sections of the Food Safety Modernization Act (FSMA). The FSMA, enacted in January 2011, is the most significant overhaul of federal food law since the passage of the Federal Food, Drug and Cosmetic Act in 1938.

A primary theme of the new law is to emphasize prevention of food contamination by establishing new practices in food manufacturing. New rules that result from the law will apply to all food sold in the United States, including imported food. Dietary supplement companies are exempt from some parts of the law, and these exemptions also apply to both domestic and foreign firms. (See the [AHPA Update](#) of Dec. 20, 2010.)

The focus of the meetings was on the pending implementation of some of the elements of FSMA Title III, Improving the Safety of Imported Food. More specifically, the March 29 meeting was titled, [FSMA](#)

“A primary theme of the new law is to emphasize prevention of food contamination by establishing new practices in food manufacturing.”

[and Imports: A New Paradigm for Importers](#), while the March 30-31 meeting was called, [Ensuring the Safety of Imported Foods and Animal Feed: Comparability of Food Safety Systems and Import Practices](#).

■ "During the meetings, FDA staff stressed the risk-management nature of the new law, which requires FDA to efficiently use its resources and focus testing and regulation efforts on high-risk foods and food ingredients while continuing to monitor low-risk products at a lower rate."

The meetings provided an opportunity to discuss FSMA Section 301 (Foreign Supplier Verification Program), which, as of January 2013, will require all food importers to verify that the foods they import are manufactured in compliance with US laws and are not adulterated. Sections 302 (Voluntary Qualified Importer Program), 305 (Building Capacity of Foreign Governments), and 307 (Accreditation of 3rd-Party Auditors) were also addressed in some detail. Representatives from FDA explained that the latter section will require accredited auditors to notify FDA of conditions that "could cause or contribute to a serious risk to the public health," during both regulatory and consultative audits, and welcomed further comments and suggestions to clarify the exact scope of this section of the law.

During the meetings, FDA staff stressed the risk-management nature of the new law, which requires FDA to efficiently use its resources and focus testing and regulation efforts on high-risk foods and food ingredients while continuing to monitor low-risk products at a lower rate.

Throughout the meetings, the agency stressed that it would respect all US trade obligations to treat foreign producers and importers on an equitable level with domestic producers. It also communicated its understanding of the potential impact of new costs on small businesses and stated its intention to minimize these while still meeting its goals. FDA also promised that any new importer requirements would be clearly announced well in advance of compliance dates.

"It is reassuring to see FDA's commitment to cooperation and communication with industry," notes AHPA President Michael McGuffin. "This new law is going to meaningfully change the way that food importers operate, and it is essential that we pay attention to the agency's implementation strategies."

An [archived webcast of the March 29 meeting](#) has been released by FDA. The agency says it is preparing transcripts of both events.

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FDA Convenes Second FSMA Meeting: Preventative Controls of New Food Safety Law; AHPA Plans Comments

By Merle Zimmermann, AHPA Information Analyst.

The Food and Drug Administration (FDA) continued its series of educational meetings to discuss components of the Food Safety Modernization Act (FSMA). An April 20, 2011, session focused on Preventative Controls.

A primary theme of the new law is to emphasize prevention of food contamination by establishing new practices in food manufacturing. New rules that result from the law will apply to all food sold in the United States, including imported food. Dietary supplement companies are exempt from some parts of the law, and these exemptions also apply to both domestic

and foreign firms. (See *AHPA Updates* of [Dec. 20, 2010](#) and [April 15, 2011](#).)

The focus of this meeting in the ongoing series was Preventative Controls, a topic in FSMA Title I, *Improving Capacity to Prevent Food Safety Problems*. Preventative Controls are used by facilities to identify and address hazards associated with specific foods and food processes and discussed in FSMA Section 103. Two main themes recurred through the meeting: risk assessment for individual products and how facilities can learn about and apply preventative controls in their own manufacturing business.

At the meeting, FDA representatives inquired what industry in each field considers “high risk” and “low risk” food products and ingredients, noting “We were intentionally vague in what we said ... [to allow industry to] ... categorize foods [itself].” FDA’s goal to leverage preexisting organization and knowledge in fulfilling its food safety goals was especially clear in this area, and the agency said it welcomes comments on how best to define high and low risk products.

In answer to inquiries about FDA releasing guidance documents to better explain the terminology in the law and intentions of the regulation, the agency embraced this idea and offered to prepare particular documents immediately after inquiries were received. Also mentioned were possible educational guidance documents showing general examples of how preventative controls and Hazard Analysis Critical Control Point (HACCP) requirements apply in actual situations. FDA also stated that it would consider guidance documents from international bodies such as Codex Alimentarius during development of new regulations.

The agency expressed interest in working with industry in conducting safety training for small businesses to further compliance goals, though it had no clear comments when it was suggested FDA accredit domestic third-party educational and auditing programs for that purpose.

FDA reiterated its desire for information on preventative-control best practices from existing large

businesses and trade associations.

“FDA’s continued commitment to involving industry in the regulatory process is refreshing,” says American Herbal Products Association (AHPA) President Michael McGuffin. “As this new law impacts policy and procedure from seed to shelf, FDA’s desire for businesses and trade associations to be integrally responsible for our own regulatory frameworks will allow for minimal disruption to industry while meeting FSMA’s new prevention goals.

“AHPA remains committed to ensuring the highest quality and consumer confidence in dietary supplements and manufacturers, and we intend to participate in the FSMA implementation process throughout its development,” he adds.

FDA is accepting general written comments on FSMA through June 30, 2011, and AHPA’s Government Relations Committee continues to review the process in the interim. Please contact [Michael McGuffin](#) if you have any suggestions or would like to participate in AHPA’s review.

The [FDA website for the April 20 event](#) includes an agenda, and FDA indicates that a copy of the webcast will be made available for viewing there as well.

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GAO Calls for FDA Inspection Authority on Food Claims Records

By Michael McGuffin, AHPA President.

In a report issued in January, the Government Accountability Office (GAO) recommended that the Food and Drug Administration (FDA) request Congress amend current law to provide FDA with the authorities needed to inspect the evidence that companies use to support structure/function and other claims made on food. GAO made the recommendation so that FDA could “establish whether there is scientific support for

■ "The GAO report is focused entirely
■ on claims made on conventional
■ foods and does not address
■ dietary-supplement claims."

the claims." In the report, GAO also recommends that FDA provide guidance to industry on the type and strength of scientific evidence needed to prevent false or misleading information in a structure/function claim for a food, and that the agency provide direction to its inspectors so that they can better identify potentially false or misleading structure/function claims on food products.

The [GAO report](#) is titled: *FDA Needs to Reassess its Approach to Protecting Consumers from False or Misleading Claims*. It is addressed to Sens. Daniel Inouye, D-HI, and Thad Cochran, R-MS, the chairman and ranking member of the Senate Committee on Appropriations, respectively; and to Reps. Harold Rogers, R-KY, and Norman Dicks, D-WA, who hold these positions on the U.S. House of Representatives' Committee on Appropriations.

The GAO report is focused entirely on claims made on conventional foods and does not address dietary-supplement claims. It discusses the issue of qualified health claims in great detail, and in fact may be worth reading for no other reason than for its thorough treatment of this subject. In reviewing the use of structure/function claims on conventional foods, the report notes FDA's position that such claims may only be based on a food's nutritive value, and reiterates that, unlike the stricter requirements for dietary supplements, food companies are not required to notify FDA or use disclaimers when they make structure/function claims.

In recommending that FDA seek congressional authority to inspect claim-substantiation records, GAO notes that the Federal Trade Commission (FTC) already has such authority for advertising claims. GAO also reports that FTC has "taken enforcement actions for

alleged false structure/function claims on food labels and in advertisements." The GAO report does not address why FDA should also have authority to inspect food company records since FTC has shown that it is willing to act against companies for claims made not only in advertising but also on product labels.

GAO reports that FDA stated that it would work to determine whether it needs additional statutory authority to inspect food-claims records and that it would consider providing guidance to the food industry on the type of evidence needed to substantiate structure/function claims. On this last point, GAO notes that FDA already has such [guidance for dietary supplements](#), and that the agency "could issue a statement that the same principles apply to foods."

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FDA Issues First Reportable Food Registry Report

By Anthony L. Young, Esq., Partner, Kleinfeld, Kaplan and Becker, LLP, and AHPA General Counsel.

The Food and Drug Administration (FDA) has released a new report detailing its experience with its Reportable Food Registry (RFR) during the Registry's first year of existence. The annual report, the [Reportable Food Registry Annual Report](#), is a synopsis of the one-year reporting period from Sept. 8, 2009, through Sept. 7, 2010. It is an extension of the [Reportable Food Registry Interim Seven-Month Report](#) issued in July 2010, which covered the reporting period Sept. 8, 2009, through March 31, 2010.

The RFR was part of the FDA Amendments of 2007. A reportable food is an article of food/feed for which there is a reasonable probability that the use of, or exposure to, such article of food will cause serious adverse health consequences or death to humans or animals. All foods under FDA's jurisdiction, including animal feed/food and pet food, may be reportable foods, except for dietary supplements and infant formula.

■ "Of note to the botanical industry, 17 of the primary RFR entries involved spices and seasonings, 16 involved nut and seed products, 14 related to raw agricultural commodities, and eight involved stabilizers, emulsifiers, flavors and colors."

On its website, FDA characterizes the report as:

... a measure of our success in receiving early warning on problems with food and feed. The data in this report represent an important tool for targeting our inspection resources, bringing high-risk commodities into focus, and driving positive change in industry practices—all of which will better protect the public health.

Reporting under the RFR has mainly related to the presence of pathogens. During the period of this first annual report, FDA received 2,240 reportable submissions. Of those, 229 were primary reports (226 were industry primary reports and three were regulatory primary reports submitted voluntarily by federal and state regulatory officials); 1,872 were subsequent reports as a result of a primary report; and 139 were amendments to previously submitted primary or subsequent reports. The 229 primary RFR entries included 201 concerning human food and 28 concerning pet food and animal feed.

■ "The net conclusion of FDA and the food industry is that this law is working to address food safety issues before they reach the consumer."

Of note to the botanical industry, 17 of the primary RFR entries involved spices and seasonings, 16 involved nut and seed products, 14 related to raw agricultural commodities, and eight involved stabilizers, emulsifiers, flavors and colors—all ingredients that are used or are similar to those that are used in botanical dietary supplements. Salmonella was the safety hazard predominantly reported in all these categories. The largest RFR incident involved hydrolyzed vegetable protein. Here is what FDA reported:

Hydrolyzed Vegetable Protein (HVP): A food manufacturing facility received a shipment of a flavor enhancer, HVP, which tests showed to be positive for Salmonella Tennessee. The facility submitted a reportable food report to FDA identifying the problem and its supplier. FDA conducted a risk control review analysis and consulted with both the primary report submitter and the supplier. The supplier voluntarily recalled the product and submitted a reportable food report. FDA requested that the supplier notify the immediate subsequent recipients of the reported HVP, which helped FDA identify the many other recipients of the ingredient. FDA worked with the recipients to address their specific situations. This resulted in: 177 products containing the recalled HVP being removed from commerce as of the date of this report. No illnesses associated with the recalled ingredient have been reported.

The HVP recall was responsible for 1001 RFR entries, most of them in March 2010 involving at least 11 different commodity categories.

What is noteworthy regarding this HVP situation is that no illnesses were reported, and 117 products were removed from commerce. This involved FDA tracking all users of the HVP in question and then pressuring them to either recall the product or face press releases from FDA stating that they were not cooperating with the agency. The net conclusion of FDA and the food industry is that this law is working to address food safety issues before they reach the consumer.

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of any user or endorser of a product or service, including, but not limited to, misrepresenting that (s)he is an independent user or ordinary consumer of the product or service. In addition, Legacy must disclose clearly and prominently a material connection, when one exists, between itself and the person promoting its program.

More importantly, the order imposes on Legacy the duty of establishing, implementing and maintaining a system to monitor its affiliates' endorsements and disclosures. Under this system, Legacy must monitor its top 50 revenue-generating affiliates on at least a monthly basis in a manner reasonably calculated not to disclose the source of the monitoring activity at the time it is being conducted. For the remaining affiliates, the order requires similar monitoring of a random sample of 50. Legacy must immediately terminate any affiliate that poses as an ordinary consumer or fails to disclose the existence of a material connection to Legacy. Finally, Legacy must create and maintain records of its monitoring program. Like all FTC administrative orders, the order will remain in effect for 20 years. Legacy is liable for civil penalties if it violates the order, up to \$16,000 per day, per violation.

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Given this case and FTC's continued interest in the use of testimonials and endorsements—particularly in online advertising—now would be a good time for companies to review their use of these techniques in advertising and to ensure that they require endorsers to disclose whether they are receiving payment or other compensation for their product reviews and testimonials.

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Dear Retailer: **There's a Hole in the cGMP Bucket** **Industry needs to fix the problems in the regulations regulating repackaged supplements, or we can expect FDA to fix them—badly**

By Anthony L. Young, Esq., Partner, Kleinfeld, Kaplan and Becker, LLP, and AHPA General Counsel.

When the Food and Drug Administration (FDA) promulgated Good Manufacturing Practice (cGMP) for dietary supplements, it provided special treatment for those who "package or label a product that [is received] for packaging or labeling as a dietary supplement (and for distribution rather than for return to the supplier) ... " [21 CFR §111.75(e)]. This section of the regulation establishes the important requirements for determining whether dietary-supplement manufacturing specifications have been met. In §111.75(c) and (d) there are specific requirements for accomplishing this. But for those who package or label already-manufactured dietary supplement products, all that is required is for the packager or labeler to "visually examine the product and have documentation to determine whether the specifications that you established under §111.70(f) are met." In turn, all that the section requires are specifications "to provide sufficient assurance that the product you receive is adequately identified and is consistent with your purchase order."

In a Petition for Reconsideration filed July 25, 2007, the American Herbal Products Association (AHPA) sought reconsideration for this part of the cGMP, among others. In its petition, AHPA expressed concern that

■ “The continuing concerns about
 ■ products spiked with prescription
 ■ weight-loss or erectile-dysfunction
 ■ drugs, illegal steroids, or their
 ■ analogs highlight the size of the
 ■ hole in this bucket.”

this section would invite “for example, an unscrupulous packaging company to attempt to skirt the Final Rule by hiding their responsibility to be certain of the identity, purity, strength and composition of the dietary supplements that they sell behind this paragraph, or a manufacturing company to take advantage of their knowledge that their customers’ obligations to ensure product quality is limited by this paragraph.”

The continuing concerns about products spiked with prescription weight-loss or erectile-dysfunction drugs, illegal steroids, or their analogs highlight the size of the hole in this bucket. Labelers and packagers in the United States can receive finished product for labeling or packaging, set minimum specifications, package, label, and ship a product and claim: “we had no idea” the product was spiked. So what is the solution? Perhaps it is time for the retail community to use its powers to assure that products in these classes meet the standards intended by FDA in its guidance regarding dietary supplements. Retailers can and should ask hard questions about products that are in the categories that FDA identified in the December 15, 2010, letter to industry as the most likely candidates for spiking—those promoted “for weight loss, sexual enhancement, and body building.”

Questions to ask: Where were the capsules or tablets manufactured? If the answer is a US manufacturer, then follow-up would be appropriate. If the answer is an offshore manufacturer, then the packager or labeler should be quizzed on how it was established that the product is not spiked. And there are a myriad of other questions that might be asked. Why should retailers take these steps? The easiest and

most obvious answer is to demonstrate the industry’s responsibility to ensure that consumers receive dietary supplements that are not adulterated or misbranded and that deliver what they claim to deliver—and not less than they claim—and certainly in the case of these highly scrutinized categories, not more than they claim.

But what about the products that are marketed as supplements and sold in back rooms, on disappearing and reappearing websites, and out on the streets? These marketers are not representative of or even a part of our industry, and they should remain isolated in their illegal pursuits.

What might FDA do? There already exist special cGMPs for low-acid canned foods, juice products, and seafood because these products can pose special risks to consumers. Where products pose special risks, FDA can and has established special cGMPs. The dietary supplement industry’s goal should be to address the problem so FDA does not find it necessary to create a solution that sweeps up, for example, multivitamins formulated for men’s special health needs, weight-loss supplements that have a long track record of safety, and sports- nutrition products generally.

As is and has been the case in many other industries and classes of consumer products, the best solution to any problem in our industry is the solution we impose on ourselves. Self-regulation certainly beats the alternative.

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What the Warning Letters Teach: A Demand for Compliance

By Anthony L. Young, Esq., Partner, Kleinfeld, Kaplan and Becker, LLP, and AHPA General Counsel.

The Food and Drug Administration (FDA) Warning Letters are instructive because they disclose those matters that FDA has determined it would follow through on if the company receiving the letter does not come into compliance. A Warning Letter is a demand for compliance. The American Herbal Products Association (AHPA)

notifies its members about Warning Letters for dietary supplements and botanical food products in Legal Alerts because these letters provide key information about the agency's enforcement priorities. Any regulated industry wants to see where enforcement occurs. Why? Because these industries are generally compliant with regulatory mandates, and those companies operating outside the regulatory boundaries are competing unfairly by using unlawful methods to sell their products.

■ "Putting those claims on a website
■ makes a company an easy target
■ for a desktop inspection by FDA."

With every large-scale natural disaster, including the recent earthquake and resultant tsunami in Japan, the US marketplace seems to be flooded by quick cures and "complete" protections offered by the dietary supplement and other industries. In this case, FDA quickly alerted consumers—and in so doing, it also alerted the supplement industry—about products fraudulently making claims regarding exposure to radiation-emitting materials from the damaged nuclear reactors. Despite fair warning, two dietary supplement companies made unlawful claims for their potassium iodide products and thus were each the recipient of a Warning Letter: [Eidon Inc.](#) and [KT Botanicals LLC](#).

On another note, the April 6 Warning Letter to [Omega Nutrition USA](#) teaches the vagaries of FDA inspections. The company received only one warning with respect to good manufacturing practice (cGMP). The letter stated that Omega Nutrition's master manufacturing records were not compliant—the company was using a recipe-calculator sheet in lieu of detailed specifications and controls for each product. Later, FDA identified structural failures in the design of the facility, as well. The Warning Letter also noted that products did not bear the term *dietary supplement* and that the company website made numerous drug claims for products.

[Saw Palmetto Harvesting Co.](#) received a Warning

Letter after FDA performed a desktop inspection of the company's website. Claims that products will address erectile dysfunction and address benign prostatic hypertrophy resulted in a Warning Letter. Putting those claims on a website makes a company an easy target for a desktop inspection by FDA.

It is unlawful to make unapproved drug or health claims for foods. So, labeling sprouts and mung beans and other foods as potent anti-tumor agents or as reducing the risk of breast cancer resulted in a Warning Letter, as [Jonathan's Sprouts Inc.](#) found out. Moreover, unapproved antioxidant and vitamin-nutrient-content claims also deserved a warning in FDA's view. This letter is instructive in that it demonstrates when nutrient content claims may and may not be made.

A similar Warning Letter went to [Diaspora Tea & Herb Co. LLC](#) with respect to unlawful drug and nutrient content claims. Dietary supplement companies need to be attentive to nutrient-content-claim regulations and requirements. Such claims are not the highest FDA priority, but when FDA sees that they are being made, the agency will act as it did in these cases.

It is important for even the most experienced companies to assure that relevant personnel are reading and familiar with FDA Warning Letters. Following the AHPA Legal Alerts is one way to do so. IASC members can sign up their employees for these alerts by providing names and email addresses to Devon Powell via [email](#). In this fashion, both new and old, and experienced and inexperienced employees can keep up to date with FDA enforcement activities.

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Industry Hosts First Dietary Supplement Caucus Briefing for the 112th Congress

The Congressional Dietary Supplement Caucus (DSC), in cooperation with the leading trade associations representing the dietary supplement industry—the American Herbal Products Association (AHPA), the Natural Products Association (NPA), the Council for Responsible Nutrition (CRN), and the United Natural Products Alliance (UNPA)—held its first briefing for the 112th Congress on April 6. A capacity crowd of 60 House and Senate staffers attended this event.

“AHPA is pleased to be part of this cooperative process, and to provide information to Congressional offices to keep them well informed on supplement issues,” says Michael McGuffin, AHPA president.

The luncheon briefing featured Mark Blumenthal, founder and executive director of the American Botanical Council. “I’m truly grateful and honored for this invitation to talk about how safe and beneficial dietary supplements support the health of our citizens and save our nation billions in health care costs each year,” says Blumenthal. “The excellent turnout among Congressional staffers demonstrates the increasing interest in and importance of dietary supplements on Capitol Hill.”

Among the key points of Blumenthal’s presentation:

- ◆ Half of all Americans use dietary supplements, according to the *Journal of Nutrition*.
- ◆ Dietary supplements are regulated as foods under the Dietary Supplement Health and Education Act of 1994 (DSHEA).
- ◆ The industry has a strong record of self-regulation, including:
 - ◆ AHPA’s establishment of standards for nomenclature and guidelines for safety
 - ◆ CRN’s multi-year grants to the Council of Better Business Bureaus’ National Advertising

Division to help ensure truthfulness in supplement advertising

- ◆ NPA’s good manufacturing practices (GMP) program and training seminars
- ◆ UNPA’s GMP training initiative, some initiatives co-led with the University of Mississippi
- ◆ Dietary supplements have an outstanding safety record, with government statistics showing they are one of the safest categories of consumer products.

Additional briefings will be scheduled on Capitol Hill. This was the first briefing for the 112th Congress and the ninth in a series of briefings since the DSC launched in 2005.

The DSC was recently re-launched for the 112th Congress. The caucus serves as a bipartisan, bicameral group of members to facilitate discussions among lawmakers about the benefits of dietary supplements, provide tips and insights for better health and wellness, and promote research into the health care savings provided by dietary supplements.

In addition, the caucus brings Congressional attention to the role of supplements in health promotion and disease prevention, and addresses the regulation of the supplement industry. Sens. Orrin Hatch, R-Utah, and Tom Harkin, D-Iowa, and Reps. Dan Burton, R-Ind., Jason Chaffetz, R-Utah, Jared Polis, D-Colo., and Frank Pallone, D-N.J., serve as co-chairs of the caucus.

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