AHPA REPORT

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In this issue of the *AHPA Report*

You Need to Know

New Members

- **Ginseng Board of Wisconsin** Our mission is to represent Wisconsin Ginseng producers as the worldwide leader of the American Ginseng industry. We are committed to the advertising, promotion and the sale of Wisconsin Ginseng, the purest ginseng in the world. We work to improve the health and wellness of consumers while supporting the sustainability of the industry and rural economy associated with it. Our objectives are accomplished through education, research, and expanding international & domestic markets. Website: *www.ginsengboard.com* ■

AHPA Responds to JAMA Study on Ginkgo, Cognitive Decline

An article published in the Dec. 29 issue of the *Journal of the American Medical Association* reports that *Ginkgo biloba* extract is ineffective in reducing cognitive decline in older adults with normal cognition or with mild cognitive impairment.

The article released presents the findings of a secondary analysis of data from the randomized double-blind Ginkgo Evaluation of Memory (GEM) study, the results of which were published in November 2008. The original GEM trial followed 3,069 individuals of age 75 or older assigned to either placebo or 120 mg twice-daily ginkgo extract (Schwabe's EGb 761®). The primary outcome analysis of the original GEM study found *Ginkgo biloba* extract ineffective for preventing dementia even though the incidence of development of dementia was lower than expected, and 40 percent of the active group was not compliant in taking their ginkgo.

This week's publication involved a review of the data generated in the original GEM study to see if ginkgo slowed the rate of cognitive decline in the study participants. "The data review conducted for this article suffers from the same limitations as the original GEM study with an additional challenge due to the testing schedule not being ideally suited for this new endpoint," said American Herbal Products Association (AHPA) Chief Science Officer Steven Dentali, Ph.D.

"Furthermore, as with the primary findings of the GEM study, the findings of the secondary analysis in no way undermines what has already been observed with regard to the usefulness of ginkgo extract, and EGb 761 in particular, in providing symptomatic relief in persons who already suffer from dementia or Alzheimer's disease. Also what has not yet been published, but is clear from a review of the study data, is that the common supposition of increased risk of bleeding from EGb 761 ingestion turns out not to be true," said Dentali (*See the AHPA Update of Nov. 18, 2008 for more information*).

The abstract of the JAMA study is here: *http://jama.ama-assn.org/cgi/content/abstract/302/24/2663*.

AHPA's response to the finding of the 2008 GEM study is here: *http://www.ahpa.org/Default.aspx?tabid=69&aId=495&zId=1* ■

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Message from the President

Michael McGuffin

AHPA President Michael McGuffin Looks Ahead to 2010

Dear AHPA Members,

Over the past three years, the herbal products industry has experienced two landmark events: the passage of the Serious Adverse Event (SAE) Reporting law and the promulgation of Good Manufacturing Practice (GMP) regulations for dietary supplements. In 2010, these will remain important new factors in the industry as the remaining companies (50 employees and under) become subject to GMPs and the second full year of mandatory SAE reporting is completed. Food and Drug Administration (FDA) and Federal Trade Commission (FTC) enforcement and pending legislation in the U.S. Congress are also likely to be newsmakers for the industry in the coming year.

When the American Herbal Products Association (AHPA) first petitioned FDA for mandatory SAE reporting, we did so with the confidence that this obligation would demonstrate the safety of our class of goods. AHPA has been filing Freedom of Information Act (FOIA) requests for SAER data on dietary supplements, and data shows the confidence in the safety of dietary supplements was far from misplaced. In calendar year 2008, 1,025 reports of adverse events associated with dietary supplements were reported to FDA. Only about eight percent of these reports were associated with herbal dietary supplements (i.e, a product containing only one herb or a combination of herbs or where the primary ingredient is an herb or a combination of herbs). Overall, data show companies are submitting SAEs to FDA, and the total number of reports for this class is low.

At this point in time, meeting GMPs seems to be a learning process for both FDA and industry. FDA inspectors are still undergoing training on the new regulations in some districts; some inspectors are giving food GMP inspections but identifying what they will be

looking for in a dietary supplement inspection. AHPA encourages members to contact us and inform us of your experiences with GMP inspection. This information will help us develop our communications to FDA and tools for industry, such as our recent guidance document on dealing with an FDA inspection.

The change in administration has brought a new enforcement environment. In the past year, FDA has identified several classes of products (male virility, weight loss and sports) unlawfully marketed as "dietary supplements" that FDA acknowledges are illegal drugs. It is apparent from enforcement actions around the globe that the problem of spiking in these classes is international. AHPA has suggested FDA use its effective and efficient strategy against fraudulent H1N1 products against products that are labeled as dietary supplements but claim to contain illegal steroids. This would not catch all the bad guys, but it would pick off the low hanging fruit.

Companies that manufacture products in these categories may also consider proactive approaches to ensuring that their products do not inadvertently contain these ingredients. 21 CFR 111 requires companies to test raw materials for known contaminants in ingredients. Also, companies must have specifications to provide sufficient assurance that the product received is adequately identified and is consistent with the purchase order. The FDA Act is a strict liability statute. It is a crime to sell an illegal drug, even if you don't "know" you're doing it.

In Congress, some form of food safety legislation will pass this coming year. Companies should expect such legislation to grant FDA more power to detain potentially unsafe products, and possibly to order recalls. In general, with regards to DSHEA and legislation specific to our class of goods, we need to remain vigilant but dietary supplements are not the present focus of food safety legislation – the focus is on the food.

The coming year is bound to be an exciting one for our industry, as well as the food and healthcare industries at large. AHPA is looking forward to serving our members through all the developments of 2010 and beyond. I wish you and your families a happy, healthy and prosperous new year!

Sincerely,

Michael McGuffin
President
American Herbal Products Association

Special Topics

Supplements in Liquid Form: The New Draft Guidance and AHPA's Comments Past and Future

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

Well, the liquid supplement shoe may be dropping. The Food and Drug Administration (FDA) has, after ten years, issued a Draft Guidance[1] on the subject and sent three letters[2] to try to "make a record" regarding the policy direction FDA now wishes to take. The letters are unusual in that two respond to New Dietary Ingredient (NDI) notifications filed many years ago – indicating FDA staff hunted for example products to write about and expended quite some effort looking for those examples.

In the new Draft Guidance, FDA provided the following examples as factors the agency will consider in determining that a liquid product is a dietary supplement or conventional food:

- "the packaging of liquid products in bottles or cans similar to those in which single or multiple servings of beverages like soda, bottled water, fruit juices, and iced tea are sold, suggests that the liquid product is intended for use as a conventional food."
- "Liquid products that suggest through their serving size, packaging, or recommended daily intake that they are intended to be consumed in amounts that provide all or a significant part of the entire daily drinking fluid intake of an average person in the U.S., are represented as beverages."
- "Product or brand names that use conventional food terms such as "beverage," "drink," "water," 'juice," or similar terms represent the product as a conventional food."

These are big and bold assertions that the dietary supplement industry needs to consider and to measure against products presently on the market and how those products may deviate from the parameters FDA proposes. Comments may be submitted on the Draft Guidance by Feb. 2, 2010. The American Herbal Products Association (AHPA) Government Relations Committee will be considering whether to make comments, and the nature of any comments AHPA may make to FDA, between now and then. AHPA members with views on this subject should contact AHPA President and Government Relations Committee Staff Liaison Michael McGuffin (301-588-1171 x201; *mmcguffin@ahpa.org*).

[1] Draft Guidance available online at *http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm192702.htm*

[2] Letters to industry available online at *http://www.fda.gov/Food/DietarySupplements/GuidanceComplianceRegulatoryInformation/ucm192981.htm*

The Draft Guidance also addresses the subject of so-called "novel" ingredients added to liquid products that are labeled as conventional foods. FDA points out that dietary ingredients that are not generally recognized as safe (GRAS) or approved food additives may be added to dietary supplements but that "any substance added to a beverage or other conventional food that is an unapproved food additive (e.g., because it is not GRAS for its intended use) causes the food to be adulterated under section 402(a)(2)(C) of the FFDCA." This means that such ingredients must be approved food additives or GRAS, including GRAS self-affirmed, prior to their use in conventional foods.

Finally, the Draft Guidance summarizes the rules relating to labeling claims for conventional foods, such as health claims, nutrient content claims, and structure/function claims, specifically noting that "if a structure/function claim promotes a [conventional food] product for a use other than providing taste, aroma or nutritive value, such as blocking the absorption of carbohydrates in the gut, the claim may cause the product to be a drug by changing its primary use."

The Draft Guidance may be a response to a January 2009 Government Accountability Office Report[3] on dietary supplements that called out this issue in a section entitled, "The Boundary between Dietary Supplements and Foods with Added Dietary Ingredients Is Not Always Clear":

"The boundary between dietary supplements and foods containing added dietary ingredients is not always clear. FDA officials have noted, for example, that a tea with an identical mix of herbal ingredients could be considered either a dietary supplement or a food product. FDA determines how to classify the tea based on the product labeling. More specifically, according to FDA, if the tea is labeled as a dietary supplement and is not represented as a conventional food, FDA would consider the tea to be a dietary supplement and regulate it as such. On the other hand, if the tea is labeled as a food or is represented as a conventional food with terms such as "drink" or "beverage," FDA officials noted that they would consider the tea to be a food.

The way FDA classifies a product is important because the safety standard that applies to the product varies based on that classification. If the product is classified as a conventional food, the added dietary ingredient must meet the GRAS standard or be approved by FDA as a food additive, except in certain circumstances as authorized in law. If the product is classified as a dietary supplement, the added dietary ingredient is presumed safe if it was marketed in the United States before October 15, 1994; otherwise, it is considered a new dietary ingredient, and the manufacturer or distributor may be required to notify FDA 75 days before the product with the added dietary ingredient enters the market and provide some basis for concluding that the ingredient is reasonably expected to be safe. According to FDA and industry officials, this is a less

[3] The Jan. 29, 2009 GAO Report "Dietary Supplements: FDA Should Take Further Actions to Improve Oversight and Consumer Understanding" is available online at *http://www.gao.gov/products/GAO-09-250*.

stringent standard than that for food additives. However, FDA does not have the authority to require that the safety of dietary supplements be approved before entering the market.

These differences in how products are regulated may lead to circumstances when an ingredient would not be allowed to be added to a product if it was labeled as a conventional food but would be allowed in the identical product if it was labeled as a dietary supplement. This was the case, for example, in August 2007, when FDA identified a company marketing an iced tea mix containing stevia—an herb that had not been approved as a food additive because of potential safety concerns, including reproductive and cardiovascular effects. FDA issued a warning to the company; however, rather than discontinue using stevia in its product, the company changed the label to classify the product as a dietary supplement rather than a food, and the product remains on the market. We identified other products that also fall within the gray area between dietary supplements and foods with added dietary ingredients that are being marketed as dietary supplements. For example, we identified several nutrition bars, teas, and energy drinks, some produced by large companies with national distribution, which contain herbs such as kava, St. John's wort, and echinacea. If these ingredients are added to conventional foods and are not GRAS and have not been approved as food additives, then they would violate the Federal Food, Drug, and Cosmetic Act. An FDA official told us that FDA is unaware of a basis for concluding that these ingredients are GRAS, and they have not been approved as food additives. However, these products may remain on the market because they are labeled as dietary supplements. Such a process might allow companies to circumvent the safety standard required for food additives.

In FDA's 10-year plan to implement DSHEA, issued in January 2000, the agency identified the need to clarify the boundary between conventional foods and dietary supplements but did not indicate when or how the agency planned to address this issue. Moreover, we highlighted this particular issue in our July 2000 report and recommended FDA take action to clarify the boundary between conventional foods and dietary supplements. As of November 2008, the agency had not issued regulations or guidance to clarify this boundary.

In its Draft Guidance, FDA does not refer to the 2009 GAO Report, nor does FDA refer to its prior effort to obtain comments on this category. As one of its 1999 Program Priorities, FDA had identified the "boundaries between dietary supplements and conventional foods, between dietary supplements and drugs, and between dietary supplements and cosmetic products," as matters to be considered. And in a *Federal Register* notice of June 18, 1999, FDA invited comments on these matters. AHPA's comments on the conventional food issues can be found here: h*ttp://www.ahpa.org/Portals/0/pdfs/_99_0820_AHPAComments_Boundary_Food_Supp.pdf.*

AHPA also addressed the issue of boundaries between conventional foods and dietary supplements in a meeting with FDA officials in July 2001. AHPA's focus was on herbal supplements in beverage form. AHPA's concern emanated from warning letters FDA had written to beverage manufacturers regarding the use of botanicals in conventional food form beverages. That meeting was followed by a July 17, 2001 letter,[4] articulating AHPA's then and present position on the subject and the material that follows is taken from that letter.

AHPA's position is that herbal supplements may be marketed in conventional food form so long as the product is represented as a supplement and not represented as a conventional food. When supplements are in conventional food form, they have different labeling and content requirements than conventional food. They are set forth below:

Dietary Supplement in Conventional Food Form	Conventional Food
1. The term Dietary **Supplement** or Herbal **Supplement** appears as the statement of identity on the principal display panel.	1. A statement of identity describes the food, e.g., apple juice, on the principal display panel.
2. Nutrition labeling is titled **Supplement Facts**.	2. Nutrition labeling is titled **Nutrition Facts**
3. Dietary ingredients for which RDI's and DRV's have not been established must be declared by their common or usual name and their quantitative amount by weight presented in the **Supplement Facts** panel.	3. Non RDI or RDA ingredients are listed in ingredient labeling only, and not in **Nutrition Facts**, and are not required to be quantified.
4. Dietary ingredients must be reasonably expected to be safe but are not required by DSHEA to be approved food additives, GRAS listed or GRAS self-affirmed.	4. All ingredients must be approved food additives, GRAS listed or GRAS self-affirmed.
5. Structure function statements must bear the **DSHEA disclaimer**.	5. Structure function statements need not bear the DSHEA disclaimer.

[4] AHPA's July 17, 2001 letter is available here: *http://www.ahpa.org/Portals/0/pdfs/01_0717_FoodSupp_Boundaries_Letter_Lewis.pdf*

AHPA's position is that consumers purchasing properly labeled dietary supplements in conventional food form receive more information about the products they buy than do consumers of conventional food. Moreover, products labeled as dietary supplements are plainly distinguished by their supplement statement of identity, their Supplement Facts panel and the fact that they quantify the amount of each dietary ingredient in the product.

It has long been the law that a manufacturer, through labeling, determines the category (food, dietary supplement, drug or cosmetic) in which its product is marketed. Dietary supplement type products in beverage form, especially as powders to be added to or converted to liquids, were on the market when DSHEA was passed. And while there is no official legislative history on the point, beverages and bars were the intended beneficiaries of the category that was created by DSHEA's amendment of the definition of dietary supplement.

In its written response to AHPA's 2001 meeting with and letter to FDA,[5] the agency advised (in relevant part) that –

The Dietary Supplement Health and Education Act (DSHEA) of 1994 amended the Federal Food, Drug, and Cosmetic Act (the Act) to define and establish a framework for regulating "dietary supplements." These amendments essentially permit dietary supplements to be similar to conventional foods in composition and form. However, the definition for a "dietary supplement" under DSHEA excludes products represented as conventional foods and distinguishes dietary supplements from conventional foods in many important ways, e.g., different requirements with respect to safety, to the types of claims that can be made, and to the kind of information that must be provided in the nutrition label.

Among other things, in order to be regulated as a dietary supplement, the product must bear the term "dietary supplement" as part of its common or usual name. This term may be modified to include the name of the dietary ingredient. Dietary supplements must also bear a "Supplement Facts" label unless they are exempt from nutrition labeling. However, whether a product is regulated as a dietary supplement or conventional food represented for use as a conventional food, or as a sole item of a meal or the diet. Even if a product is labeled as a dietary supplement, representations that the product serves as a substitute for a conventional food subjects the product to regulation as a conventional food.

The FDA does not object to a dietary supplement being marketed with the physical attributes that are essentially the same as a conventional food as long as the dietary supplement product is accurately labeled and not represented for use as a conventional food. The FDA will continue to object to products represented for use as conventional foods that are labeled as "dietary supplements." The agency's position on this issue has been articulated in the preamble to the final rule for Dietary Supplements (62 Federal Register 49826 at 49862).

A product may be "represented for use as a conventional food," in part, by statements and/or vignettes that appear on the label and that suggest the product is or can substitute for a conventional food. The use of a standardized food name (e.g., spring water or orange juice) on a dietary supplement or conventional food suggests that a product is or can substitute for the standardized food, and thus represents the product for use as a conventional food. The use of a traditional food term (e.g., drinks, beverages, cereals, spreads, soups, breakfast drink) on a dietary supplement or conventional food also suggests that a product is or can substitute for a conventional food. The use of a vignette that depicts a product in a conventional food setting (e.g., a bowl of cereal, hot chocolate) and the physical location of the product in the marketplace can suggest that the product is or can substitute for a conventional food.

FDA's Draft Guidance is not far off from the position FDA took in its 2001 response to FDA. In the interim, there has been substantial growth in the liquid dietary supplement category. Those who are in this category need to examine FDA's Draft Guidance carefully to ascertain how it impacts their products. ■

[5] FDA's Nov. 8, 2001 letter to AHPA is available here: *http://www.ahpa.org/Portals/0/pdfs/01_1108_Foret_FoodSupp_Boundaries.pdf*

What Does the National Toxicology Program (NTP) Have to Do With the Herbal Products Industry?

By Katia Fowler, Director of Communications, AHPA

Four years after the passage of the Dietary Supplement Health & Education Act (DSHEA), the Department of Health and Human Services' National Toxicology Program (HHS/NTP) hosted an "International Workshop to Evaluate Research Needs on the Use and Safety of Medicinal Herbs."[1] In addition to concerns that "herbal formulations are not subject to Food and Drug (FDA) premarket toxicity testing" and that usage had "increased substantially" post-DHSEA,[2] NTP held the workshop because over the past several years it had received a number of nominations for herbs – mostly, if not all, by federal agencies.

In January 1998, NTP recorded goldenseal (*Hydrastis canadensis*), and constituents berberine and hydrastine; comfrey (*Symphytum officinale*); and saw palmetto (*Serenoa repens*) as new nominations for study by NTP. These herbs were nominated by the National Institute of Environmental Health Sciences of the National Institutes of Health (NIEHS/NIH). Following the workshop, the National Cancer Institute (NCI) in 1999 nominated several more herbs for testing: aloe vera (*Aloe vera*), ginseng (*Panax* spp.), kava (*Piper methysticum*) and milk thistle (*Silybum marianum*).[3]

[1] Description available at *http://ntp.niehs.nih.gov/index.cfm?objectid=06F61238-E0BB-FD4F-E08DDB63E69442CC#HERBS http://www.niehs.nih.gov/news/releases/news-archive/1998/herbsfin.cfm*

[2] NTP's 2006 "Medicinal Herbs: Fact Sheet": *http://ntp.niehs.nih.gov/ntp/Factsheets/HerbalFacts06.pdf*

[3] NTP's Dec. 18, 2009 *Management Status Report* (MSR) does not include comfrey and saw palmetto: *http://ntp.niehs.nih.gov/ntp/msr.pdf*. The MSR gives the status of those NTP agents selected for Study in one or more of the standard 2-week, 13-week, and/or 2-year Toxicology and Carcinogenicity Protocols.

Since the late '90s additional herbs and herbal compounds have been accepted for study by NTP including black cohosh (*Actaea racemosa*), bladderwrack (*Fucus vesiculosus*), *Echinacea purpurea* extract and bitter orange (*Citrus* × *aurantium*). Several months ago, during a July 2009 meeting, NTP's Board of Scientific Counselors recommended the program move forward with toxicological studies on dong quai (*Angelica sinensis*) root and extract. Whether or not this herb will be selected for study by NTP will be determined by the NTP Executive Committee. Evening primrose (*Oenothera biennis*) oil, butterbur (*Petasites* spp.), and valerian (*Valeriana oficinalis*) extract and oil are also awaiting review by the NTP Executive Committee.[4]

While new herbs are being nominated, toxicological studies on herbs accepted for study over a decade ago are wrapping up and results are under review for publication as NTP Technical Reports and peer-reviewed journals. This year, the American Herbal Products Association (AHPA) filed several comments on NTP's Technical Report on goldenseal (*see p. 12 for more on this story*). In addition, the International Aloe Science Council (IASC) is actively working to prepare for the publication of NTP's findings on aloe vera.[5]

In light of the recent activity, this article is meant to serve as a source of information on NTP and its relevance to the herbal products industry. It also aims to inspire AHPA's active and associate member companies to become involved in the association's NTP-related work. Member companies interested in learning more about AHPA's efforts should contact AHPA President Michael McGuffin (301-588-1171 x201; *mmcguffin@ahpa.org*).

What is the National Toxicology Program (NTP)?

The Department of Health and Human Services (HHS) established NTP in 1978 to "coordinate toxicological testing programs within the Department; develop and validate improved testing methods; and provide information about potentially toxic chemicals to health regulatory and research agencies, the scientific and medical communities and the public."[6]

NTP is an inter-agency program composed of the National Institute of Environmental Health Sciences of the National Institutes of Health (NIEHS/NIH), the National Institute for Occupational Safety and Health of the Centers for Disease Control and Prevention (NIOSH/CDC), and the National Center for Toxicological Research of the Food and Drug Administration (NCTR/FDA).

NTP writes that it has "developed an increasingly interactive relationship with regulatory agencies. Through this relationship, the NTP plays an important, although indirect role in shaping public health policy."

Who nominates substances and how does NTP decide which to study?

Anyone can nominate substances for testing by NTP, including the public, federal and state agencies, international and non-governmental organizations, labor groups (occupational safety issues), industry and academia. In actual practice, however, it is often government entities that nominate substances for testing.

Each nomination undergoes several layers of review before being selected for testing. Nominations are preliminarily reviewed by representatives from federal agencies on the Interagency Committee for Chemical Evaluation and Coordination (ICCEC) and made available to the public for review and commentary. Next, an external advisory body to NTP, the NTP Board of Scientific Counselors reviews the nominations and public comments. A decision on whether to recommend the chemical for further study is made by the NTP Board of Scientific Counselors during an open public meeting. The final decision to proceed with testing is made by the NTP Executive Committee.

NTP identifies the following nomination principals for NTP studies:

- Chemicals found in the environment and not closely associated with a single commercial organization
- Biological or physical agents that may not be adequately evaluated without federal involvement
- Commercial chemicals with significant exposure that were first marketed prior to current testing requirements or those that generate too little revenue to support further evaluations
- Potential substitutes for existing chemicals or drugs that might not be developed without federal involvement
- Substances that occur as mixtures for which evaluations cannot be required of industry
- Chemicals or agents that will aid the understanding of chemical toxicities or an understanding of the use of test systems to evaluate potential toxicities
- Chemicals that should be evaluated to improve the scientific understanding of structure-activity relationships, and thereby help limit the number of chemicals requiring extensive evaluations
- Emergencies or other events that warrant immediate government evaluation of a chemical or agent

[4] To check the status of a nomination, visit NTP's "Nomination Status Search" Web page: *http://ntp.niehs.nih.gov/?objectid=9BEB6C5F-F1F6-975E-7D3F691C4A24FC33*.

[5] IASC is an independent trade association managed by AHPA. AHPA's Chief Operating Officer, Devon Powell, serves as Executive Director of IASC. IASC's activities in response to the pending publication of NTP's findings are discussed in the association's newsletter: *http://www.iasc.org/insidealoe.html*. For more information, contact Devon Powell (*dpowell@iasc.org*; 301-588-2420).

[6] NTP's 2001 "Current Directions & Evolving Strategies" *http://ntp.niehs.nih.gov/ntp/Main_Pages/PUBS/NTP2001CurrDir.pdf*

Why are herbs nominated and selected for testing by NTP and what other compounds are being tested?

NTP studies a wide variety and thousands of chemicals in consumer products, environmental surroundings, the workplace, medicines and therapeutics. In addition to herbal medicines, NTP stated in 2001 it was focusing on several other areas that "have received inadequate attention in the past": photoactive chemicals, contaminants of finished drinking water, endocrine-disrupting agents, DNA-based therapies and certain occupational exposures. Recently, NTP's attention has turned to Bisphenol A (BPA), nanoscale materials and formaldehyde. Additional chemicals studied by NTP include acetaminophen (the active ingredient in Tylenol) and indole-3-carbinol, which NIEH describes in its 1999 press release as "a substance in cruciferous vegetables such as broccoli, and thought to have potential to reduce the risk of cancer."

Information provided by NTP indicates herbs have been nominated and accepted for study based on "widespread and growing" usage and as "biological or physical agents that may not be adequately evaluated without federal involvement." As noted earlier in this article, most herbs have been nominated for study by federal agencies and a concern is repeatedly cited that FDA pre-market toxicity testing is not required of herbal medicines prior to marketing.

In a February 2009 document entitled, "Looking Deeper: How Today's Research is Building a Safer Tomorrow,"[7] NTP describes an interest broadened to dietary supplements in general. NTP writes:

> Once a product is marketed, the FDA has the responsibility for monitoring safety and must show that a dietary supplement is not safe before it can take action to restrict its use or remove it from the marketplace. The NTP is working closely with the FDA to address questions about the safety of a broad range of dietary supplements including:
>
> - Multipurpose and miscellaneous use supplements (e.g., goldenseal and milk thistle)
> - "Women's health" supplements (e.g., black cohosh)
> - Cancer chemoprevention supplements (e.g., green tea and resveratrol) "Anti-aging" supplements (e.g., Ginkgo biloba and ginseng)
> - Weight loss aids and sports supplements (e.g., bitter orange and androstenedione[8])

[7] Available online at *http://ntp.niehs.nih.gov/files/NTP_CurrentDirectionsBrochure_Final_508.pdf*

[8] Editor's Note: Androstenedione products marketed as dietary supplements are in fact unapproved drugs, as clearly established by FDA in 2004. See *http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108262.html* and *http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/ComplianceEnforcement/ucm081788.htm*

Who oversees the testing process and how does it work?

Following selection for study by NTP Executive Committee, NTP designs and initiates studies based on "resources, priorities, and knowledge gaps." Substances may be studied for a variety of health-related effects, such as reproductive and developmental toxicity, genotoxicity, immunotoxicity, neurotoxicity, metabolism, disposition and carcinogenicity.

Each substance studied by NTP is assigned an NIEHS/NIH study scientist who designs a comprehensive testing strategy (design, methods, hypothesis, etc.). A project review committee evaluates the testing strategy and proposes a vehicle for execution (grant, contract, etc.).

Additionally, NTP receives external science oversight and peer review from the NTP Board of Science Counselors, the Technical Reports Subcommittee, Report on Carcinogens Subcommittee and the Advisory Committee on Alternative Toxicological Methods.

What difference does it make to my company that herbs are being tested by NTP?

NTP identifies itself as playing an important, although indirect, role in shaping public health by "providing needed scientific data, interpretations, and guidance concerning the appropriate uses of these data to regulatory agencies and other groups involved in health-related research."

NTP's scientific data, interpretations and guidance is primarily provided through the program's publications. NTP publishes longer-term studies, generally two-year rodent studies, as NTP Technical Reports and in peer-reviewed scientific journals. NTP's major publication, however, is its *Report on Carcinogens*.

For the herbal products industry, the regulatory impact of these publications would primarily be felt through California's Proposition 65, which maintains a list of chemicals "known to the state of California" to cause cancer or reproductive toxicity. Under Proposition 65's disclosure requirements, a food or dietary supplement to which a listed carcinogen is added is generally required to provide a "clear and reasonable warning" that the food "contains a chemical known to the State of California to cause cancer."

The listing of chemicals in the Proposition 65 list is overseen by the State of California's Office of Environmental Health Hazard Assessment (OEHHA). OEHHA identifies NTP as an "authoritative body" for purposes of supporting the listing of a chemical as a carcinogen or reproductive toxin. Under the law, the "formal identification" of a chemical as a carcinogen by an authoritative body is a sufficient basis for including that chemical in Proposition 65's listing. The inclusion of a chemical in NTP's *Report on Carcinogens* (RoC) is generally agreed to be "formally identifying" a chemical as a carcinogen. According to OEHHA, an NTP

Technical Report may also formally identify a carcinogen if certain criteria are met.[9]

The implication of this is that "sufficient" evidence in a Technical Report may lead OEHHA to list a substance, and in turn, require products including that substance bear a warning under Proposition 65. This may have additional public relations and legal repercussions.

What is AHPA doing to protect herbs being tested by NTP?

Goldenseal, nominated in 1997, is the first of the herbs selected in the late '90s to reach the Technical Report stage (*see p. 12 for more on this story*). In February, NTP's Board of Scientific Counselors Technical Reports Review Subcommittee held a meeting during which the draft Technical Report was reviewed. AHPA submitted written comments in advance of the meeting, and AHPA member company Gradient Corporation submitted written comments on AHPA's behalf, and at AHPA's expense. AHPA President Michael McGuffin also attended the meeting and provided oral comments. In July, NTP's Board of Scientific Counselors met to consider adopting the Technical Report on goldenseal, and AHPA again provided substantive written comments.

The AHPA Board of Trustees voted in July 2009 to form a working group to review and recommend an overall course of action in this matter. The association is monitoring the status of herbs at NTP and reviewing scientific findings made available by the program. AHPA has also initiated communication with its California counsel for Proposition 65 and several AHPA member companies specializing in toxicology and Proposition 65 issues.

How can my company help?

Please contact AHPA President Michael McGuffin (301-588-1171 x201; *mmcguffin@ahpa.org*) for more information. ■

[9] "NTP Technical Reports with findings of "clear evidence" of carcinogenic activity in at least one experiment are examined to determine whether listing via the authoritative bodies mechanism is required. In such cases, OEHHA examines the Technical Report to determine whether the technical criteria in Section 12306(e) are met. Thus, the evidence is deemed "sufficient" for listing via this mechanism if there is "an increased incidence of malignant tumors or combined malignant and benign tumors in multiple species or strains, in multiple experiments (e.g., with different routes of administration or using different dose levels), or, to an unusual degree, in a single experiment with regard to high incidence, site or type of tumor, or age at onset" (Section 12306(e))." For a complete discussion see *http://oehha.ca.gov/prop65/policy_procedure/ntptechrev.html*

Status Report: Substances Selected for Study by NTP

Herbs	MSR Status *(current as of 12/18/2009)*
goldenseal root powder	Post Peer Review Technical Reports in Progress (Short-Term Studies)
goldenseal root powder	Post Peer Review Technical Reports in Progress (Long-Term Studies)
ginseng	Post Peer Review Technical Reports in Progress (Long-Term Studies)
senna (powdered)	Long-Term Exposure Studies Scheduled for Peer Review
black cohosh	Short-Term Studies Completed: In Review for Further Evaluation
bitter orange	Chemicals Assigned to Laboratory for Toxicology/Carcinogenesis Study
Herbal Extracts	
milk thistle extract	Post Peer Review Technical Reports in Progress (Long-Term Studies)
kava kava extract	Long-Term Exposure Studies Scheduled for Peer Review
ginkgo biloba extract	Long-Term Exposure Studies: Pathology Quality Assessment in Progress
green tea extract	Long-Term Exposure Studies: Laboratory Study Report in Preparation
aloe vera whole leaf extract (native)	Long-Term Exposure Studies: Laboratory Study Report in Preparation
usnea barbata, extract ((+) -usnic acid)	Short-Term Exposure Studies in Progress
gum guggul extract	Short-Term Exposure Studies in Progress
Echinacea purpurea, ext.	Chemicals with Project Leader Assigned/Study in Design
Garcinia cambogia extract	Chemicals with Project Leader Assigned/Study in Design
Herbal Constituents	
isoeugenol	Galley or Camera Copy Technical Reports in Progress
pulegone	Post Peer Review Technical Reports in Progress (Long-Term Studies)
alpha/beta Thujone mixture	Long-Term Studies Scheduled for Peer Review
indole-3-carbinol	Long-Term Exposure Studies: Laboratory Study Report in Preparation
resveratrol	Short-Term Studies Completed: In Review for Further Evaluation
myristicin	Short-Term Studies Completed: In Review for Further Evaluation
ephedrine + caffeine combination	Short-Term Exposure Studies in Progress
vincamine	Chemicals Assigned to Laboratory for Toxicology/Carcinogenesis Study
annatto	Chemicals with Project Leader Assigned/Study in Design
arbutin	Chemicals with Project Leader Assigned/Study in Design
ephedrine alkaloid dietary supplements	Chemicals with Project Leader Assigned/Study in Design
Other Substances of Interest	
chromium picolinate monohydrate	Galley or Camera Copy Technical Reports in Progress
chitosan	Short-Term Exposure Studies Scheduled for Peer Review
zinc carbonate, basic	Long-Term Exposure Studies: Laboratory Study Report in Preparation
Glucosamine hydrochloride + chondroitin sulfate	Short-Term Exposure Studies in Progress
glucosamine	Chemicals Assigned to Laboratory for Toxicology/Carcinogenesis Study
chondroitin sulfate	Chemicals with Project Leader Assigned/Study in Design

The complete Dec. 18, 2009 *Management Status Report (MSR)* is available online: http://ntp.niehs.nih.gov/ntp/msr.pdf. The MSR gives the status of those NTP agents selected for Study in one or more of the standard 2-week, 13-week, and/or 2-year Toxicology and Carcinogenicity Protocols. The MSR does not provide a definition of the terms provided above under "MSR status." However, the MSR groups substances into one or more of 17 ordered status possibilities (called "reference numbers" in the MSR). "Galley or Camera Copy Technical Reports in Progress" is the highest status (Ref. No. 14) represented on this list, meaning this substance is nearest to having a printed Technical Report and/or printed Study Reports. "Chemicals with Project Leader Assigned/Study in Design" is the lowest status (Ref. No. 2) on this list. If a substance appears under more than one status level, the highest level is provided in the chart above. Long-term studies are studies of more than one year. Short-term studies are one year or less in duration.

Report on the Status of NTP's Technical Report on Goldenseal

By Michael McGuffin, President, AHPA

The National Toxicology Program (NTP) at the National Institute of Environmental Health Sciences (NIEHS) issued in December 2008 a draft Technical Report on the Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (*Hydrastis canadensis*) in F344N Rats and B6C3F1 Mice (Feed Studies).[1] This draft was reviewed at a meeting of NTP's Board of Scientific Counselors[2] (BSC) Technical Reports Review Subcommittee on Feb. 25, 2009 at the NIEHS offices in Research Triangle Park. This subcommittee voted to accept the conclusions of the draft technical report that there is "clear evidence of carcinogenic activity" for goldenseal root in the studied male and female rats, and "some evidence of carcinogenic activity" in the studied male mice. During a meeting held July 23-24, 2009, the full BSC, which serves in an advisory capacity to NTP, accepted the report on goldenseal root powder.

The American Herbal Products Association (AHPA) submitted written comments in advance of the February BSC Technical Reports Subcommittee meeting, and Gradient Corporation submitted written comments on AHPA's behalf, and at AHPA's expense. In addition, I attended the meeting and provided oral comments on AHPA's behalf. In July, AHPA submitted follow-up comments for consideration before the BSC.

NTP's Draft Technical Report

The draft technical report records the results of several studies conducted by NTP on goldenseal root in rodents, including short-term (2 week and 3 month) and long term (2 year) studies, and the researchers' conclusions as drawn from the 2 year studies.

The 2 year study included 4 groups of 50 animals of each species and gender (juveniles at onset) in each of four goldenseal root doses: 0 (controls); 3,000 ppm of feed (0.3 percent); 9,000 ppm (0.9 percent); and 25,000 ppm (2.5 percent). Upon sacrifice at the end of the study complete histopathology was performed on all animals. The number of incidences of neoplasms or nonneoplastic lesions at each specific anatomic site was recorded for each group and statistical analysis was performed. The draft technical report focused its attention on trends (some significant) in increased neoplasms or nonneoplastic lesions in the liver, and on the fact that one male rat (in the highest dosage) was observed to have developed a carcinoma.

The conclusions of the 2 year study are recorded in the draft as:

> Under the conditions of these 2-year feed studies, there was *clear evidence of carcinogenic activity* of goldenseal root powder in male F344/N rats based on the increased incidences of hepatocellular adenoma and hepatocellular adenoma or carcinoma (combined). There was *clear evidence of carcinogenic activity* of goldenseal root powder in female F344/N rats based on the increased incidence of hepatocellular adenoma. There was *some evidence of carcinogenic activity* of goldenseal root powder in male B6C3F1 mice based on the increased incidences of hepatoblastoma and multiple hepatocellular adenoma. There was *no evidence of carcinogenic activity* of goldenseal root powder in female B6C3F1 mice exposed to 3,000, 9,000, or 25,000 ppm goldenseal root powder in feed for 2 years. Administration of goldenseal root powder resulted in increased incidences of nonneoplastic lesions in the liver of male and female rats and male mice.

The categories of evidence when used by NTP, which "refer to the strength of the experimental evidence and not to potency or mechanism," are defined as:

- Clear evidence of carcinogenic activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- Some evidence of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
- Equivocal evidence of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemical related.
- No evidence of carcinogenic activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- Inadequate study of carcinogenic activity is demonstrated by studies that, because of major qualitative or quantitative limitations, cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

AHPA's February 2009 Written Comments

AHPA's written comments were addressed to the issue of the draft technical report's characterization of the level of human exposure to goldenseal root, and to the purported "overlap" of the human exposure level and the rodent exposure concentrations used in the 2-year studies.

[1] Available at *http://ntp.niehs.nih.gov/files/562_board_WEB.pdf*

[2] According to NTP, "the BSC provides scientific advice to the Director for the NTP and evaluates the scientific merit of the NTP's intramural and collaborative programs": *http://ntp-server.niehs.nih.gov/?objectid=720164A4-BDB7-CEBA-F5B86E9B53D26DED*

NTP's draft technical report identified human exposure to goldenseal root at a daily dosage level of 3 grams, and referenced the Natural Standard Databases (NSD) to support this. A review of the NSD monograph on goldenseal root disclosed that this dosage information was not supported by any reference, but simply stated as fact.

On the other hand, the American Herbal Pharmacopoeia (AHP) monograph on goldenseal root identifies the daily dose of goldenseal as 2 grams, and provides a reference to the *National Formulary* (1946). AHPA's comments suggested that AHP and its dose of 2 grams should be substituted for NSD and its 3 gram dose. NTP staff subsequently requested a copy of the AHP monograph, which was provided electronically with AHP's permission.

AHPA's written comments also stated that humans do not use goldenseal for 730 consecutive days, as had the test animals. And in my oral testimony I was able to make the point that this period of time in mice should be compared to lifetime exposure in humans.

Gradient's Written Comments

AHPA contracted with AHPA Member company Gradient Corporation to provide a review of the NTP draft technical report, and to prepare comments to identify any flaws in the draft and counter its conclusions, if such counter-position could be supported scientifically. Leslie Beyer, M.S., DABT, served as the primary point of contact at Gradient, and Gradient's review, dated February 22, 2009, was prepared by Beyer and by Mara Seeley, Ph.D, DABT, and Lorenz Rhomberg, Ph.D. Gradient's review was submitted by AHPA to NTP and was accepted as separate written comments.

Gradient's document summarized its review as follows:

> These classifications [in the NTP draft report, i.e., of "clear evidence" and "some evidence" of carcinogenicity in rats and male mice"], however, are not appropriate, because the one significant increase in carcinomas observed in the entire study (one hepatocellular carcinoma at the high dose in a male rat), is within historic control incidence. In addition, while increased incidences of hepatocellular adenomas were observed in both sexes of rats and in male mice, the adenomas were not associated with carcinomas. Elevation of adenomas without an associated increase in carcinomas (as compared to mere tumorigenicity) is much weaker evidence of carcinogenicity. For goldenseal, there are no excess hepatocellular carcinomas in mice, despite excess adenomas, casting doubt on the general presumption that the liver adenomas observed can progress to carcinomas. Thus the classifications of carcinogenic activity (based on liver neoplasms), are made without any compelling elevation in liver carcinomas.

Gradient's review provided an in-depth discussion to support its view that the NTP classification are inappropriate and concluded with the following summary list of reasons why these are not appropriate:

- Only one significant increase in carcinomas was observed in the entire study (one hepatocellular carcinoma at the high dose in a male rat), and this incidence is within historic control incidence.
- Both the increased incidence of hepatocellular adenomas in male and female rats, and the increase in combined incidence of hepatocellular adenomas or carcinomas in male rats, are only significant at the highest dose tested. The associated dose-response curves resemble hockey sticks is that the standard term?, which is consistent with a threshold response. A threshold response is also supported by the lack of mutagenicity of goldenseal, as reported by NTP.
- While hepatocellular adenomas were observed in both sexes of rats and in male mice, these adenomas were not associated with carcinomas.
- In male mice, the increased incidence of single adenomas or the combined incidence of animals with single and multiple adenomas, was not significant at any single dose (the statistical analysis is not provided for multiple hepatocellular adenomas).
- Similarly the increased incidence of hepatoblastomas in male mice was not significant at any single dose.
- The increased incidence of hepatocellular tumors in mice consists solely of benign tumors.
- There was a lack of concordance between the time-to-first-tumor and dose for hepatocellular adenomas, hepatocellular adenomas or carcinomas, and hepatoblastomas in male mice. In no case (related to neoplastic effects in the liver) was the shortest time-to-first-tumor associated with the high dose.
- There is no clear relationship between the neoplastic and the non-neoplastic events observed in rats and male mice.
- Goldenseal may have an overall protective effect with respect to neoplastic effects, as indicated by decreased incidence rates of multiple endpoints in both male and female rats, and in male mice.

Decision of the NTP Subcommittee

NTP's Technical Reports Review Subcommittee initiated its review of the draft technical report on goldenseal root with a presentation by the report's lead study scientist, June Dunnick, Ph.D. Dr. Dunnick included a reference to the use of goldenseal root by children (Barnes, 2008) and to the fact that it is one of the ten most commonly used herbs (Blumenthal, 1999).

The subcommittee next heard from individual reviewers on the subcommittee:

- Tracie Bunton, D.V.M., Ph.D. (Toxicology Consultant, Eicarte LLC) identified the report as providing a "clear presentation" and documenting a "clear progression with time"

of increased liver lesions. She suggested that AHPA's comment regarding the accuracy of references for human exposure should be checked. Dr. Bunton stated that she agrees with the draft's conclusions.

- Justin Teeguarden, Ph.D. (Senior Research Scientist, U.S. Department of Energy, Pacific Northwest National Laboratory) commented that the draft provided good documentation that dose selection was done correctly and commented that he is "leery" of very high dose studies since "I know how these studies are used." Dr. Teeguarden expressed his opinion that it would be "absolutely crucial" to understand the relationship of the test amounts to human lifetime exposure and suggested that such information should be included in the final report's conclusions. He also expressed appreciation for how the draft analyzed the noted improvement (negative trend) in fibroadenomas in the mammary gland in all exposed groups of females and suggested that other areas in which improvement was observed be similarly addressed. Dr. Teeguarden concluded by expressing his agreement with the draft's stated conclusions.
- James Sherley, M.D., Ph.D. (Senior Scientist, Programs in Regenerative Biology and Cancer, Boston Biomedical Research Institute) stated that, while it may be accurate that the test animal doses may "overlap" human exposures, as stated in the draft, the final report should clearly state the unlikelihood of such overlap in various human dose scenarios.

The subcommittee chair (Raymond Novak, Ph.D. Institute of Environmental Health Sciences, Wayne State University) then provided time (7 minutes) for submission of my oral commenta. Dr. Novak noted that the committee had already accepted the two written comments submitted by or on behalf of AHPA. I reiterated that the human exposure to goldenseal should be recorded as 2 grams per day, rather than at 3 grams as stated in the draft technical report. I also stated that, while AHPA's written comments had noted that humans do not consume goldenseal for 730 consecutive days, it would be more meaningful, since the test animals were fed goldenseal root every day over their entire lifetime, to note that humans do not consume goldenseal for every day during their entire lifetime. I also called the subcommittee's attention to the conclusions in Gradient's review and asked that these all be considered in their own review process and called particular attention to the fact that Gradient identified references that were not identified in the draft technical report that characterize the background incidence of carcinomas in rats at 0 to 2 percent, which is the same incidence observed in the highest test group (1 in 50 male rats in the highest dosage group).

Dr. Dunnick replied to the comments of the reviewers and to the oral comment by stating that she will add the AHP goldenseal root monograph to the report's references. She stated that since goldenseal is found in "over-the-counter" products there is no way to know how much is used by humans. She stated that the work of NTP is a "hazard identification study" and is not a "risk assessment," which she said is "up to the regulators." Another NTP staff scientist stated that no carcinomas had been observed in male rats in the control groups in the last 6(?) NTP-conducted studies, representing an incidence of 0 percent in 300(?) animals.

A conversation among the subcommittee ensued[3] during which Dr. Dunnick agreed to add one or two sentences into the final report's abstract to address human exposure (rather than have that information found only in the body of the text).

The subcommittee then voted to adopt the conclusions of the draft technical report as stated.

AHPA's July 2009 Comments

AHPA's written comments submitted for consideration by the BSC communicated the following points:

- TR 562 should not be adopted as a final Technical Report, or the decision to adopt should be delayed, until the conclusions presented in the draft are reconsidered. That reconsideration should include a review of any of the information provided by AHPA on Feb. 17, 2009 and by Gradient Corporation on AHPA's behalf on Feb. 22, 2009 that has not yet been completely reviewed. In addition, new information provided here on the background rate of hepatocellular carcinomas in control F344 rats that was not available to the TRRS at its February meeting should also be considered.
- The final version of TR 562 should clearly state, as was clearly stated at the Feb. 25 TRRS meeting, that the evidence of carcinogenic activity reported is not in any way a commentary on whether goldenseal root is carcinogenic in humans, and in fact does not indicate whether goldenseal root is or is not carcinogenic in humans.
- The final version of TR 562 should be reviewed to make sure that all of the questions and requests for clarification that were presented at the Feb. 25, 2009 meeting of the TRRS and for which NTP staff agreed to provide answers or clarification are included.
- AHPA is concerned that the written transcript of the discussion of TR 562 at the February 25 meeting of the TRRS, as posted online at *http://ntp.niehs.nih.gov/index.cfm?objectid=CDFCB19B-F1F6-975E-7B73393ACA9E7AA4*, is inconsistent with the actual conduct of this section of the meeting, as recorded in the video posted at *http://ntp.niehs.nih.gov/ntp/meetings/2009/trrs/20090225/videos/02-TR562.mov*.

The BSC accepted the report, as presented by the subcommittee, without the discussed clarifying language. Further, following the meeting NTP staff removed the video recording from the NTP Web site.

Next Steps

As discussed in the previous article, the relationship betwee NTP and California's Proposition 65 is of significant interest. AHPA is therefore in communication with its California counsel for Proposition 65 and several AHPA member companies specializing in toxicology and Proposition 65 issues. A working group of AHPA member companies (currently consisting of companies that donated $5,000 or more to cover expenses related a toxicological review of the Technical Report on goldenseal) is working to review and recommend an overall course of action in this matter. For more information on the issue or to become involved with the working group please contact Michael McGuffin (301-588-1171 x201; *mmcguffin@ahpa.org*).

AHPA's July 2009 comments to NTP's BSC are available online at *http://www.ahpa.org/portals/0/members/09_0723_AHPA_Comments_NTP.pdf* ■

[3] See addendum (when completed) for additional details. One point: Dr. John Bucher of NIEHS asked that it be recognized that the conclusions of evidence of "carcinogenic activity" does not mean that there is evidence of carcinogenicity.

Legal & Regulatory Update

Are You in Compliance? OIG Finds Significant Problems with FDA's Food Facility Registry

According to a Department of Health and Human Service's Office of Inspector General (HHS/OIG) report released on Dec. 11, almost half of 130 domestic food facilities surveyed by OIG failed to provide accurate information for the Food and Drug Administration's (FDA) Unified Registration and Listing System ("the food facility registry"). Additionally, five percent of the facilities failed to register with FDA, and two percent did not cancel their registration when required under the law.

The food facility registry was established by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 ("the Bioterrorism Act") and requires that certain food facilities – including AHPA member companies engaged in the manufacturing, processing, packing, or holding of dietary supplements and dietary ingredients – provide certain specified information to FDA to help the agency (1) readily locate facilities during an outbreak of foodborne illness; and (2) locate these facilities for inspection. Retailers, restaurants and transporters are among the narrow group of exempt entities.

"Proper registration under the Bioterrorism Act helps FDA find the source of contamination during an outbreak of foodborne illness and remove contaminated products from the supply chain," said AHPA President Michael McGuffin. "AHPA encourages companies to confirm the accuracy of their registrations, properly inform and train employees in this obligation and provide optional contact information to FDA as appropriate."

According to OIG, 52 percent of managers (67 of 130) at the surveyed facilities were either unaware of FDA's registry requirement (5 of 67) or unaware the law required them to update the information in the registry within 60 days of a change in the facility's information (62 of 67).

The most frequent pieces of information that were either inaccurately or not reported by companies were:

- Contact information for the facility
- Emergency contact phone number
- Contact information for the owner or operator
- Contact information for the parent company

OIG writes, "Facility managers most commonly reported that they failed to provide FDA with accurate information either because they

did not update the information for the registry as required; they incorrectly entered the information during the initial registration; or the responsibility for maintaining the registration was transferred to another person who mistakenly reregistered the facility." OIG also notes several facilities had multiple registrations for the same facility.

The Registration of Food Facilities Regulation is provided in the OIG report: *http://oig.hhs.gov/oei/reports/oei-02-08-00060.pdf*.

FDA's guidance document, "What You Need to Know about the Registration of Food Facilities," is available here: *http://www.ahpa.org/Portals/0/pdfs/03_1100_FDA_RegistrationGuidance.pdf*.

For additional requirements under the Bioterrorism Act see the AHPA Web site: *http://www.ahpa.org/Default.aspx?tabid=238*. ■

Warning Letters

For the benefit of our members, AHPA notifies members of new Warning Letters posted on FDA's Web site. Below AHPA General Counsel Anthony L. Young, Esq. (Kleinfeld Kaplan & Becker) reports on the significance of several recently-issued Warning Letters. Warning Letters are first distributed to AHPA members who subscribe to the AHPA Legal Alert service. For more information, email Katia Fowler, *kfowler@ahpa.org*.

Two Warning Letters to Nestlé Teach Caution on Claims for Toddler Beverages, Medical Foods

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

Nestlé has received two warning letters from the Food and Drug Administration (FDA) regarding products marketed to parents for children. First, Juicy Juice Brain Development Fruit Juice Beverage and other Juicy Juice products were challenged for making unauthorized nutrient content claims – such claims are not allowed for products intended for use by infants or children under the age of two. The unauthorized nutrient content claim that was challenged was "no sugar added" and "naturally lower in sugar." FDA also objected to some of the flavor designations. Interestingly, having addressed these issues, FDA did not comment on the propriety, from a regulatory perspective, of the Brain Development trade name and claim. *http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm194122.htm*

The second letter to Nestlé involved BOOST Kid Essentials Nutritionally Complete Drinks promoted as "medical foods" to address the medical condition of "failure to thrive" and for "pre/post surgery, injury or trauma, chronic illnesses." FDA noted that these BOOST products do not meet the definition of "medical food" and that the claims being made are drug claims and that the product is not approved as a drug. The letter pointed out the requirements

that a product must meet to be a "medical food" under the Orphan Drug Act and noted that "there is no evidence that patients with the medical condition of 'failure to thrive' have distinctive nutritional requirements or unique nutrient needs. In addition, there is no distinctive nutritional requirement for 'pre/post surgery, injury or trauma, chronic illnesses,' as the nutritional requirements of individuals with these conditions vary greatly based on the specific circumstances of each individual."
http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm194121.htm

AHPA members in the main market their products as foods or dietary supplements. The first letter to Nestlé has important teachings for those who market products to children under the age of two. The second letter is another teaching, the first came in a Warning Letter in November to Pan American Laboratories: the medical foods category is very narrow and FDA has a newly renewed interest in the boundaries established in the law for this category.
http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm191841.htm ■

Quick Round-up

For the benefit of our members, AHPA keeps an eye on the many agencies that regulate the herbal products industry. Below are several recent regulatory developments that may interest you. They were first sent to those AHPA members who subscribed to the AHPA Legal Alert. For more information, email AHPA's Katia Fowler, *kfowler@ahpa.org*.

Consumers are warned not to buy bogus products marketed as 'herbal' treatments for erectile dysfunction

Evidence from around the world suggests that such products are often adulterated with random quantities of pharmaceutical substances, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) announced Dec. 16. Risks can include serious harm and even death. The only authorized products to treat erectile dysfunction are sildenafil, tadalafil, and vardenafil which must be prescribed by a doctor and dispensed from a pharmacy. Any product obtained by other means is considered illegal. Consumers are taking major risks if they purchase these products, writes MHRA.
http://www.mhra.gov.uk/Howweregulate/Medicines/Herbalmedicines/HerbalSafetyNews/Currentsafetyissues/CON065616

FDA Letters to Industry: Factors that Distinguish Liquid Dietary Supplements from Beverages

FDA posted three letters to industry on a new Web page on Dec. 7. The letters (sent to three companies: Coolwater Trim, Skinny Nutritional, and Burren Springs) address factors that distinguish liquid dietary supplements from beverages.
http://www.fda.gov/Food/DietarySupplements/GuidanceComplianceRegulatoryInformation/ucm192981.htm

Gov't auditors say food-tracing program flawed

A crucial part of the nation's rapid-response plan – the ability to trace food through the supply chain during an illness outbreak or bioterrorism attack – is seriously flawed, an independent watchdog agency has found, the Associated Press wrote Dec. 11.
http://www.wtop.com/?nid=104&sid=1837249

[*Editor's Note: A direct link to the OIG report is here: http://oig.hhs.gov/oei/reports/oei-02-08-00060.pdf. For more information on the report see story on p. 16.*]

USDA and HHS Continue Food Safety Working Group Efforts; Customs and Border Protection Opens Import Food Safety Center

Agriculture Secretary Tom Vilsack and Health and Human Services (HHS) Secretary Kathleen Sebelius on Dec. 9 commended the Department of Homeland Security for opening a center devoted to ensuring the safety of foods imported to the United States. The Commercial Targeting and Analysis Center (CTAC) for Import Safety is operating under the direction of Customs and Border Protection (CBP). It was created on the recommendation of President Obama's Food Safety Working Group, which is charged with advising the President on how to upgrade the U.S. food safety system for the 21st century.
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm193668.htm

Food Label Makeovers Proposed by CSPI

The Center for Science in the Public Interest announced its "expos[ure of] some of the tricks that occur on the front of the label" and a proposed makeover of the Nutrition Facts panel and ingredient lists" in its *Nutrition Action Healthletter*. CSPI campaigned for the 1990 law requiring nutrition labeling – the Nutrition Labeling and Education Act (NLEA).
http://www.cspinet.org/new/200912071.html

Food Defense Tool from FDA and APHIS Helps Farmers, Producers Assess Vulnerabilities

The FDA of the U.S. Department of Health and Human Services and the Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA) have created an online tool to help farmers and producers assess and mitigate vulnerabilities in their production processes, the agencies announce Dec. 4. The risk assessment tool called Agriculture CARVER + Shock is designed to help the food industry at the farm level – implement food production security methods.
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm193091.htm

[*Editor's Note: The software is free and available at http://www.fda.gov/Food/FoodDefense/CARVER.*]

Classification of Three Steroids as Schedule III Anabolic Steroids Under the Controlled Substances Act

With the issuance of a Dec. 3 final rule, the Deputy Administrator of the Drug Enforcement Administration (DEA) classified the following three steroids as "anabolic steroids" under the Controlled Substances Act (CSA):Boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione. These steroids and their salts, esters, and ethers are schedule III controlled substances subject to the regulatory control provisions of the CSA. Effective Date: January 4, 2010.
http://edocket.access.gpo.gov/2009/pdf/E9-28572.pdf

Draft Guidance for Industry: Factors That Distinguish Liquid Dietary Supplements From Beverages, Considerations Regarding Novel Ingredients, and Labeling for Beverages and Other Conventional Foods; Availability

The Food and Drug Administration (FDA) announced Dec. 3 the availability of a draft guidance entitled "Guidance for Industry: Factors that Distinguish Liquid Dietary Supplements from Beverages, Considerations Regarding Novel Ingredients, and Labeling for Beverages and Other Conventional Foods." The draft guidance describes factors that can be used to identify liquid products that are excluded from being dietary supplements because they are represented as conventional foods. Further, the draft guidance reminds manufacturers and distributors of beverages and other conventional foods, particularly those that contain novel ingredients, about the requirements of the Federal Food, Drug, and Cosmetic Act (the act) regarding ingredients and labeling.
http://edocket.access.gpo.gov/2009/pdf/E9-28926.pdf

[*Editor's Note: A direct link to the guidance is here: http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm192702.htm.* *See story p. 4 for more information.**]*

Caffeinated Alcoholic Beverages

The Food and Drug Administration (FDA) announced Nov. 13 that it has notified nearly 30 manufacturers of caffeinated alcoholic beverages that it intends to look into the safety and legality of their products. The FDA noted that it is unaware of the basis upon which manufacturers may have concluded that the use of caffeine in alcoholic beverages is GRAS or prior sanctioned. To date, the FDA has only listed caffeine as GRAS as an ingredient for use in cola-type beverages in concentrations of no greater than 200 parts per million.
http://www.fda.gov/Food/FoodIngredientsPackaging/ucm190366.htm

[*Editor's Note: AHPA is providing this link to FDA's Nov. 13, 2009 release on caffeinated alcoholic beverages because the principles discussed regarding the addition of caffeine to beverages may have applicability to those AHPA members who manufacture or distribute food products with added caffeine.*] ■

Communications Update

AHPA Media Scan: Notable "Herbal Headlines"

These "herbal headlines" – and headlines of interest to the herbal industry – have been selected from the past few weeks of media activity. If you would like a copy of any of these articles, please email Katia Fowler *kfowler@ahpa.org*.

AHPA in the News

Dec. 30, 2009 – If You Can Tell By the Label…AHPA's Call for Efficient Enforcement Against Illegal Steroid Products *Whole Foods Magazine*

Dec. 14, 2009 – Industry Targets Bogus H1N1 Claims *"The Tan Sheet"*

Nov. 30, 2009 – New cleanliness guidelines for herbal products *Nutraingredients-USA.com*

Nov. 23, 2009 – Co-Packaging Enters Gray Area As Option For OTC/Supplement Combos "*The Tan Sheet"*

Dec. 30, 2009 – If You Can Tell By the Label…AHPA's Call for Efficient Enforcement Against Illegal Steroid Products *Whole Foods Magazine*

Dec. 28, 2009 – Labeling standards for caffeine *L.A. Times*

Dec. 17, 2009 – China succeeds in developing herbal medication to treat A/H1N1 flu *Xinhua*

Dec. 17, 2009 – Universities push for better CAM training *Pharmacy News*

Dec. 10, 2009 – Three Substances to Lose Place on Store Shelves *New York Times*

Dec. 9. 2009 – Flu-Fighting Foods *CBS News*

Dec. 7, 2009 – 'Green' cuisine not always as ordered *Washington Post*

Dec. 6, 2009 – A broader definition of healthcare *L.A. Times*

Nov. 24, 2009 – Herbal remedies need real scrutiny *CNN*

Nov. 12, 2009 – Fighting illness isn't just a one-shot deal *Washington Post*

Nov. 10, 2009 – Experts: Placebo power behind many natural cures *Associated Press*

Nov. 9, 2009 – In Central Oregon, a sip of South America *The Bulletin*

Nov. 4, 2009 – Kellogg's Pulls Immunity Claims From Cereal Boxes *WCCO*

Nov. 3, 2009 – Home Flu Cures: Bad Medicine? *The Wall Street Journal*

Nov. 3, 2009 – More insurers are paying for alternative remedies *Associated Press*

Nov. 3, 2009 – Complementary and Alternative Medicine Therapies for Cold and Flu Season: What Is the Science? *Medscape*

Nov. 2, 2009 – Med, nursing schools teaching alternative remedies *Associated Press*

Oct. 27, 2009 – A dubious alternative *Washington Post*

Oct. 27, 2009 – FDA sets sights on products that purport to fight swine flu *Washington Post*

Oct. 26, 2009 – Alternative Health Care Offsets Cost Woes *CBS*

Oct. 18, 2009 – Student's Research: Energy Drinks are Bunk *CBS*

Oct. 16, 2009 – Beware of Flu Scams *The Today Show*

Oct. 14, 2009 – FDA chief: Regaining your trust *Fortune*

Oct. 14, 2009 – Chinese herbs show promise for diabetes prevention *Reuters*

Oct. 14, 2009 – FDA warns P&G over vitamin C in DayQuil and NyQuil *Reuters*

Oct. 13, 2009 – Green tea may curb risk of some cancers *Reuters*

Oct. 13, 2009 – A Vigorous Push From Federal Regulators *Washington Post*

Sept. 30, 2009 – Hallucinogenic Herb Under Legislative Eye *Washington Post*

Sept. 29, 2009 – Congress, Concerned About Steroids, Reviews Law on Dietary Supplements *The New York Times*

Sept. 9, 2009 – Harkin accepts chairmanship of HELP Committee *The Hill*

Aug. 20, 2009 – Supplement Update: Oprah and Dr. Oz Sue *CBS News*

Aug. 20, 2009 – Herbs, vitamins that can hurt you *CNN*

Aug. 17, 2009 – Herbal supplements not always safe, says Mayo Clinic *Nutraingredients-USA.com*

Aug. 12, 2009 – Customer spots poison stems in salad *Reuters*

Aug. 8, 2009 – Audit of organic program is ordered *Washington Post*

Aug. 4, 2009 – Consultation on how to regulate complementary and alternative therapies *Times Online*

Aug. 4, 2009 – Senate boosts food stamps as unemployment rises *Washington Post*

July 31, 2009 – Will Uncle Sam Pay for Your Yoga? *The Atlantic*

July 30, 2009 – House passes far-reaching food safety bill *Associated Press*

July 30, 2009 – Americans spend $34 billion a year on alternative medicine *USA Today*

July 28, 2009 – FDA warns against body-building products claiming steroids *CNN*

July 27, 2009 – FDA flexes muscle as raid sends message to supplement industry *Daily News*

July 24, 2009 – Senators seek coverage for alternative therapies *Boston Globe* ■

Calendar of Botanical Events

Many more listings are online at ***www.ahpa.org***.

- **Feb. 3-5: 2010 CIES Food Safety Conference,** Washington, D.C., Learn about how 3rd party food safety certification can benefit your company. *http://www.tcgffoodsafety.com/*

- **Feb. 16-19: Focus on the Future,** Hyatt Regency, Scottsdale, Ariz. Focus on the Future is an exclusive summit for top executives in the dietary supplement and healthy food industries looking to explore new ideas, learn about emerging trends, and establish new connections. Website: *http://www.focusonthefuture.net/2010/*

- **Feb. 17-20: BioFach 2010,** Germany. Where Organic People Meet – World Organic Trade Fair. Website: *http://www.biofach.de/en/default.ashx*

- **Feb. 23-24: Economic Analysis of Nutrition Interventions: Methods, Research and Policy,** Bethesda North Marriott Hotel & Conference Center, North Bethesda, Md., The National Institutes of Health's Office of Dietary Supplements (ODS) will host this day-and-a-half long workshop to bring together U.S. and international academicians, researchers, policymakers and regulators to address the following key areas and questions specifically as applied to nutrition interventions: (1) State of the Science: What are the health economic methods currently used to judge burden of illness, interventions or healthcare policies, and what new research methodologies are available (or are needed, i.e. what are critical knowledge or methodological gaps or barriers?); (2) Research Applications: What are the current and planned evidence-based health economic research activities in nutrition at the NIH, CDC, AHRQ, USDA, FDA, CMS, OMAR, etc. and what are the activities in other countries? and (3) Regulatory and Policy Maker Perspectives: Once these research goals have been met, how can they assist regulatory and policy makers with nutrition policy decision-making? Website: *http://ods.od.nih.gov/News/NutritionInterventionsWorkshop.aspx*

- **Feb. 25-26: Stevia World Americas,** W Atlanta Midtown Hotel, Atlanta, GA. Come to CMT's **Stevia World Americas** to gather latest information and establish new links and relationships. Regular updates of the event and other interesting industry news and reports will be available on *http://www.cmtevents.com/aboutevent.aspx?ev=100208&*.

- **March 11: Food and Dietary Supplement Immunity Claims and Enforcement,** Webinar hosted by the Food and Drug Law Institute (FDLI). Hear the relevant regulators discuss product claims along the spectrum from immune system

support, to enhancing immunity, to strengthening the immune system, to preventing colds and flu, and to preventing H1N1 influenza. Such claims currently appear in a wide variety products and in diverse contexts. Dr. Robert Moore will talk about the FDA's joint initiative with FTC against companies marketing fraudulent anti-H1N1 influenza products and about the agency's approach to more general immune system and immunity claims. Richard Cleland will discuss FTC's expanded enforcement activities involving unsubstantiated immunity and immune system boosting claims, including the FTC's recent cases against chain retailers for claims on their store brands.
Website: *http://www.fdli.org/conf/webinar/immunity/?utm_source=MagnetMail&utm_medium=email&utm_term=kfowler@ahpa.org&utm_content=FDLI%20Prospectus,%20January%2013,%202010&utm_campaign=fdli-2010-01-13*

♦ **March 11-14: Natural Products Expo West**, Anaheim Convention Center, Anaheim, Calif. Natural Products Expo West continues to be the leading trade show in the natural, organic and healthy products industry. Rated as one of the top 200 trade shows in the US by Tradeshow Week, Natural Products Expo West continues to help attendees reach their business goals in this dynamic industry.

♦ **March 21-25: 239th ACS National Meeting & Exposition, San Francisco, CA**. For further information, please contact the symposium organizers or the AGFD program chair (Michael Appell 309 681-6249 *michael.appell@ars.usda.gov*).

♦ **March 16-18, 2010: GMA Science Forum: Navigating Current Food Safety, Public Health and Lifestyle Goals,** Washington, DC. Website: *http://guest.cvent.com/i.aspx?1Q,P1,E54775F9-28DA-4F8C-A99F-27D3EDCAEE65*

♦ **March 21-25, 2010: 239th ACS National Meeting & Exposition,** San Francisco, CA. For further information, please contact the symposium organizers or the AGFD program chair (Michael Appell 309 681-6249 *michael.appell@ars.usda.gov*).

♦ **March 25-26: Sustainable Cosmetics Summit,** New York. Sustainable Cosmetics Summit is a new generation of international summits that focus on sustainability in the beauty industry. For the first time, a series of international summits examine the leading issues the beauty industry faces concerning sustainability, natural, organic, fair trade and ecological products. Hosted at the Steigenberger Frankfurter Hof hotel in Frankfurt, the inaugural summit focused on industry developments, CSR & sustainability best-practices and green formulations. ** **Call for Papers** ** The conference programme for the North America edition of the Sustainable Cosmetics Summit is currently under development. Prospective speakers should send an abstract of their papers, with full contact details by completing a registration form. *http://www.sustainablecosmeticssummit.com/*

♦ **April 8-11: AAAOM Expo 2010 - From Ancient Medicine to New Horizons,** Hyatt Regency Tamaya Resort and Spa, Albuquerque, N.M. Expo 2010 will serve as AAAOM's bridge to our 2011 "Walk on Washington" to be held in conjunction with our World Conference on Integrative Medicine, where our profession will take the lead to define AAAOM's role in U.S. healthcare as an integrative medical provider in the U.S. healthcare delivery system. As a profession, each milestone and juncture we reach forms the platform for all activity that follows. Join us in Albuquerque when we come together as practitioners, students, businesses, and educators to deepen our clinical practice skills. We will forge the unity and involvement necessary to assure that our combined expertise and knowledge will eloquently and strategically define our political path forward. Website: *http://www.aaaomonline.org/*

♦ **April 10-11: Southwest Conference on Botanical Medicine** in Tempe, Arizona. Join us for a sunny weekend in the blooming desert! Keynote speaker: Rosita Arvigo of Belize. Topics: Pelvic Decongestant Herbs; Herbal Pairing in the Vitalist Tradition; Cardiovascular Blood Markers; Uses and Cautions for Prescription-Only Botanicals; Ten Most Important Essential Oils with David Crow and much more. Preconference intensive on April 9: Women's Health: Alternatives to Statins, HPV Vaccine, Anti-depressants and Anxiolytics with Amanda McQuade Crawford. Friday Field Studies, herb walks at the Desert Botanical Garden, and outdoor classes in medicinal herb preparation. CE credits for health professionals. Information *www.botanicalmedicine.org* or (800) 252-0688.

♦ **April 12-15: 9th Annual Oxford International Conference on the Science of Botanicals**, Oxford Conference Center, Oxford, Miss. The purpose of this conference is to review, discuss, and explore the confluence of current research topics in natural product chemistry, Pharmacognosy and botanicals. Topic areas will include such issues as authentication, cultivation, collection, post-harvest practices for producing quality plant material, chemical and toxicological methods for quality/safety assessment of botanicals. Contributed presentations, both oral and poster, are invited. Each session will open with a plenary speaker outlining the current approaches, limitations, and research needs of the topic area.Speakers will be leading researchers from industry, academia, nonprofit institutions, and government. Each speaker will address current approaches, limitations, and research needs.
Website: *http://guest.cvent.com/EVENTS/Info/Summary.aspx?i=541ae65b-b5d8-407d-891d-006296d2d8d1*

♦ **April 22-23: FDLI & FDA 53rd Annual Conference**, Hilton Washington,Washington, D.C.
Website: *http://www.fdli.org/conf/#upcoming*

♦ **April 26-28: SupplySide East,** Secaucus, New Jersey. SupplySide is the world's largest trade show and conference for healthy and innovative ingredients. Thousands of decision makers from the global food, beverage, dietary supplement and cosmeceutical industries converge to learn, network, source and create. Your next big idea is just a show away.
Website: *http://www.supplysideshow.com/*

♦ **May 1: HerbDay 2010**, Nationwide. HerbDay is a coordinated series of independently produced public educational events celebrating the importance of herbs and herbalism. HerbDay was conceived of by five nonprofit organizations with interests in herbs and herbalism (the HerbDay Coalition) to raise public awareness about the significance of herbs in our lives and the many ways herbs can be used safely and creatively for health, beauty care, and culinary enjoyment. Greater familiarity with herbs will increase informed use of herbal products and build public support for maintaining personal choice in the use of botanicals.
Website: *http://www.herbday.org/index.php*

♦ **May 11-12: Food Technology, Innovation & Safety Forum 2010,** Hyatt Regency O'Hare, Chicago, IL. The 4th Food Technology, Innovation & Safety Forum 2010 brings together leading R&D, Innovation, New Product Development (NPD), Marketing and Food Safety and Quality Assurance professionals to discuss, innovate, knowledge-share and shape the future of the food industry into the new decade.
http://www.thefoodsummit.com/

♦ **May 11-13: DCAT Nutrition & Health Forum,** Desert Springs JW Marriott Resort & Spa, Palm Springs, Calif. What are the effects of the economic, political and regulatory environments on nutritional supplement manufacturers and suppliers? Find out as industry experts explore these subjects at DCAT's Nutrition & Health Forum—the must-attend networking and educational event for the dietary supplement industry. *http://dcat.org/Pages/progr_ShowProgram.aspx?IDProgram=37*

♦ **May 18-20: Vitafoods,** Vitafoods is the only event in the world to concentrate exclusively on the expanding market for nutraceuticals, cosmeceuticals, functional foods and drinks ingredients & raw materials. An annual exhibition and conference the show attracts over 8000 attendees, 500

exhibitors and 250 delegates and is regarded as the leading event in the nutraceuticals industry calendar. The 2010 edition takes place on 18-20 May 2010 at GENEVA PALEXPO, Switzerland. For more information please visit *http://www.vitafoods.eu.com/ahpa*

- **May 18-20: Finished Products Expo,** Finished Products Expo is Europe's only dedicated exhibition for manufacturers and suppliers from the dietary supplement, functional foods and functional drinks industries. The show attracts over 150 exhibiting companies and 2500 attendees from the industry and is co-located with Vitafoods, the global nutraceutical event. The only meeting place for all those within this industry, Finished Products Expo 2010 takes place on 18 - 20 May 2010 at GENEVA PALEXPO, Switzerland. For more information please visit *http://www.finishedproductsexpo.com/ahpa*

- **May 21-24: China Tea Expo,** Shanghai. For details on exhibition please contact: Shanghai Dongmao Exhibition Service Go., Ltd. Tel: 86-21-64752979 E-mail: *fulingdm@yahoo.com.cn* Contact: Mr. Yu Yang 0086-13764607886

- **June 5- 7: Medicines from the Earth Herb Symposium in Black Mountain**, NC. Annual symposium on herbal medicine at beautiful Blue Ridge Assembly near Asheville, North Carolina. Keynote speaker: Tieraona Low Dog, MD. Topics: Latest Research in Women's Health with Tori Hudson, ND; Maintaining Healthy Levels of Testosterone and Human Growth Hormone During the Elder Years; The Impact of Phytoestrogens on Breast Cancer and Reproductive Disorders and much more. Conservation of our medicinal plant heritage discussion with Rosemary Gladstar. Herb walks in the surrounding forest, medicine making and food preparation demonstrations. Preconference intensive June 4 with Tieraona Low Dog, MD. CE credits for health professionals. Information *www.botanicalmedicine.org* or (800) 252-0688.

- **June 5-8: NACDS Marketplace,** San Diego, Calif. The NACDS Marketplace Conference is not your typical trade show. It is a venue for retail buyers and sellers to meet one another and work together to bring new and innovative products to market. Where else can you have a guaranteed meeting with buyers from top retail companies? Pair this with the most expansive and timely selection of education programming in the industry and you have NACDS Marketplace. Website: *http://meetings.nacds.org/marketplace/2010/*

- **June 10-13: Food as Medicine 2010,** Capital Hilton, Washington, D.C., Food as Medicine is the most comprehensive 4 day long professional nutrition training program in the U.S. It offers the equivalent of a semester's worth of nutrition curriculum. This program provides the latest in science-based nutrition education and is designed to give graduates the knowledge, confidence and compassion required to successfully guide patients toward life-giving, healthy nutrition. Website: *http://www.cmbm.org/holistic_medicine_PROFESSIONAL_TRAINING_EDUCATION/food_as_medicine_description.php*

- **July 17-21: IFT Annual Meeting & Food Expo**, Chicago, IL. The IFT Annual Meeting & Food Expo is the ONLY annual event that brings together professionals involved in both the science and the business of food - experts from around the world from industry, academia, and government. You'll learn about the very latest trends, the newest products, and the most recent scientific innovations...and make important new professional connections. *http://www.am-fe.ift.org/cms/*

- **July 20-23: NBJ Summit**, St. Regis Resort, Dana Point, Calif. The NBJ Summit is an intimate, invitation-only networking event where top-level executives from leading companies in the health and nutrition industry discuss strategic business issues, market conditions, competitive challenges, and branding/product strategies. Over the past 12 years, The NBJ Summit has attracted key leaders and CEOs in the $100 billion dollar health and nutrition industry. This year we will present the latest *Nutrition Business Journal* market statistics with key insights for the future of the industry and how it might impact strategic planning in 2010, moving into 2011 and beyond. *http://www.nbjsummit.com/nbj10/public/enter.aspx* ■

Botanical Science Update

by Steven Dentali, Ph.D.

MEETING ATTENDED

USP Dietary Supplements – Botanicals Expert Committee

I attended the 2005-2010 Dietary Supplements – General Chapters Expert Committee on December 16, 2009 at USP Headquarters in Rockville, MD as a committee member. USP has made public recent issues before the committee including proposed general chapters on heavy metals (elemental impurities) in dietary supplements, their methods of detection, and suggested limits. The limits proposed by USP for arsenic, cadmium, lead, and mercury in finished dietary supplements as shown in the table below.

Elements	Individual Component Limit (µg/g: based on a 10 g daily dosage size)	Permitted Daily Exposure (µg/day)
Inorganic Arsenic	1.5	15
Cadmium	0.5	5
Lead	1.0	10
Total Mercury	1.5	15
Methyl-Mercury	0.2	2

These proposed limits are almost identical to those published by AHPA a year ago and which were considered by USP in their deliberations on this issue. AHPA's heavy metal guidance is available at *http://www.ahpa.org/Default.aspx?tabid=223*. AHPA's newly revised 39 page guidance document on the topic is available upon request. USP's proposed chapters can be accessed at *http://www.usp.org/hottopics/metals.html*. Public comments are due April 15 of this year.

Other revisions and new chapters before the committee include detection methods for food irradiation, screening for adulterants, probiotics standards, and setting recommended limits for pesticides in dietary supplements in collaboration with FDA, EPA, and industry. Advisory panels are likely to be convened on each of these topics to develop appropriate positions. Please let me know if you have an interest in participating.

On another note, USP revised the format of *USP 33–NF 28* to make it easier to read. Unfortunately monograph errors were introduced in the process and it is now being recalled. Originally released with an official date of May 1, 2010 the publication will be reissued with a delayed official date. Meanwhile *USP 32–NF 27* remains official. ■

LITERATURE CITATION

Smooth Move® Clinical Trial Gets Highest Possible Score

- Efficacy of traditional Chinese medicine for the management of constipation: a systematic review. Lin LW, Fu YT, Dunning T, Zhang AL, Ho TH, Duke M, Lo SK. *J Altern Complement Med.* 2009 Dec;15(12):1335-46.
- Efficacy of an herbal dietary supplement (Smooth Move) in the management of constipation in nursing home residents: A randomized, double-blind, placebo-controlled study. Bub S, Brinckmann J, Cicconetti G, Valentine B. *J Am Med Dir Assoc.* 2006 Nov;7(9):556-61.

The first citation above is a systematic review that evaluated 137 studies done on the management of constipation. Only 21 of the trials were considered "high-quality trials" for the purpose of assessing the efficacy of treatments. Of these 21, only the Smooth Move® clinical trial received the highest quality assessment score of 8 using a modified eight-item Jadad scale for methodological quality assessment. The next best rated trial received a 5.5. In other words the Smooth Move trial scored the best of all 137 studies evaluated. As for the efficacy of treatments, while the herbal treatments appear to be more beneficial than conventional medicine in the management of constipation, no definitive conclusion could be made due to the trials being so different from one another.

The second citation is the Smooth Move trial, which was conducted by AHPA member company and recipient of AHPA's 2007 Herbal Industry Leader Award, Traditional Medicinals. It compared Smooth Move tea to placebo and found that the product was significantly more (p=0.017) effective in treating constipation than placebo. On average the active treatment group had one additional bowel movement a week over the placebo group. Each single serving contains 2 grams of pharmaceutical grade herbs including 1080 mg of the stimulant laxative active ingredient senna leaf PhEur (*Cassia angustifolia* Vahl). When prepared as directed one cup of the herbal tea contains 20 mg sennosides A and B.

The other herbs in Smooth Move, in order of predominance, are bitter fennel fruit PhEur (*Foeniculum vulgare* Miller sp. *vulgare* var. *vulgare*), sweet orange peel MFR (*Citrus sinensis* (L.) Osbeck), cinnamon bark JP (*Cinnamomum cassia*

Blume), coriander fruit PhEur (*Coriandrum sativum* L.), ginger rhizome PhEur (*Zingiber officinale* Roscoe), and sweet orange peel oil PhEur (*Citrus sinensis* (L.) Osbeck) dried on acacia gum PhEur (*Acacia senegal* L. Willdenow), each of which serves a purpose in the overall formula and are traditionally combined with senna leaf. ■