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◇ IASC Staff

◇ Devon Powell,
◇ Executive Director
◇ dpowell@iasc.org

◇ Rosie Ysasi,
◇ Certification Program Coordinator
◇ rysasi@iasc.org

◇ Send inquiries, comments ◇ or requests to:

◇ International Aloe Science Council
◇ 8630 Fenton Street, Suite 918
◇ Silver Spring, MD 20910
◇ Ph: 301-588-2420
◇ Fax: 301-588-1174
◇ Email: info@iasc.org
◇ Website: www.iasc.org



DIRECTOR'S MESSAGE



The IASC has been around and going strong since the early 1980s, and in the 30+ years it's been active the aloe vera industry, it has seen many challenges, grown substantially, and very much continues to flourish—in no small part thanks to the direct efforts of the Council. Most notably, the IASC's Certification Program has contributed to the ongoing success of many aloe vera products.

The IASC Certification Program is a 3rd-party certification that ensures the content and purity of aloe vera in products via adherence to a standard of excellence that includes items such as a review of formulas, labels, marketing, and analytical analysis. The program has helped marketers differentiate their aloe vera goods for over 25 years, and the visionary leaders who developed this program should be commended for their foresight in creating and implementing it.

The program has continued to be honed since its inception and is one that not only positions products in the minds of consumers, differentiating seal-approved products from their competitors, but is also raising the bar on the manufacturing of such products with its two-pronged approach—certifying both aloe vera goods and facilities manufacturing aloe vera products to ensure the highest quality of manufacturing operations.

In order to ensure the seal continues to be recognized as it should—as a value to both marketers looking to position their products and consumers looking to purchase products of a higher quality—the IASC has been and will continue to be active in protecting the trademarked seal by taking enforcement actions against those companies using the seal without authorization. The IASC website maintains an up-to-date list of [approved products](#), making it easy for consumers to verify if a product bearing the seal is legitimate. Also listed are any products that are [no longer certified](#) as well as those the IASC has, at some time or another, become aware of that displayed the seal without authorization ([Not Certified List](#)).

Staff also welcomes and appreciates input from consumers and industry when products displaying the seal without authorization are found. In fact, it's clear from the amount of consumer requests for information on products in the program (or not in the program) that the seal's marketplace value is strong. Consumers and marketers are encouraged to send images and details to staff ([Rosie Ysasi - Certification Program Coordinator](#)) anytime a questionable product is found displaying the seal.

The IASC considers the enforcement of its seal to be such a high priority that the Board of Directors has instructed staff to register the trademark in strategic, global locations such as Mexico, China, India, Brazil, and other countries around the world, and we expect to see greater enforcement of the seal in these places as well as participation in the program as a result.

The program is open to all IASC members and non-members ([click here for an application](#) or [contact staff](#) for details or with questions). We look forward to continuing to serve the industry and consumers by offering the seal to the best possible aloe vera products available.

Devon Powell
Executive Director



Dealing with Recalls

By Marc Ullman

This is an apocryphal tale.

Once again, things have gone somewhat awry at the Really Big Vitamin Company (RBVC). The president has just been notified that, as a result of a manufacturing shift supervisor's failure to transcribe a master batch formula correctly onto a work order, RBVC has shipped several thousand bottles of JOINTZ, a glucosamine-chondroitin dietary supplement, with chitosan substituted for chondroitin.

At the same time, the president has also been handed a copy of a recent Food and Drug Administration (FDA) Letter to Industry urging companies to cease sale of dietary supplements with the ingredient comfrey. RBVC, it so happens, is the private-label manufacturer of REBOUND, an herbal dietary supplement containing comfrey designed to assist in recovery following difficult exercise or other physical stress. According to the letter, while FDA does not have scientific evidence to prove that several reported adverse events are directly linked to comfrey dietary supplements, the adverse events are consistent with reported adverse reactions in the scientific literature. FDA's letter specifically recommends that all comfrey products be withdrawn from the market immediately.

The president now has to decide what to do: 1.) Does RBVC conduct a recall of JOINTZ or REBOUND? 2.) Does it simply correct the manufacturing problem and allow JOINTZ to stay on the market? 3.) Does it continue to manufacture REBOUND, since it has received no notices of adverse events and is only the contract manufacturer? If the president decides to remove either or both of the products from the market, does RBVC notify FDA of the situation? Does RBVC need to alert its customers and/or consumers to these problems?

The only clear cut answer for the president is that he cannot simply leave these products on the market. First, he has been confronted with a formulation error

that has put an essentially untreated shellfish derivative that can cause severe allergic reactions in the product, JOINTZ, which is not labeled with any allergen warnings. Second, another product, REBOUND, contains an ingredient that FDA has specifically identified as a potential source of adverse events.

Recall vs. Withdrawal

REBOUND and JOINTZ will not necessarily have to be treated the same way. A careful reading of the FDA comfrey letter reveals that the agency has suggested that affected products be withdrawn from the market—not recalled. This is a crucial difference that can greatly affect both the advisability of FDA notification and the complexity of RBVC's effort in removing the products from the market. Unlike a recall, the withdrawal of a product from the market is not an official or formal action subject to FDA regulation. Market withdrawals can occur at a company's discretion without FDA involvement. This may allow the company to avoid any negative publicity that would be associated with an official recall (recalls are published weekly in the FDA Enforcement Reports).

Simply initiating a product withdrawal, however, may subject the company to greater liability. Because recalls are publicized, there are fewer product-liability risks for a company that initiates a recall as opposed to a mere withdrawal. After a recall is initiated and the company has fully complied with FDA recall policies, the company may be able to insulate itself from consumer claims by showing that all the dangers have been publicized and that all the necessary steps to protect the public have been taken in accordance with FDA regulations. This protection, however, is not available where the company engages in a product withdrawal.

In the case of comfrey, the FDA "industry letter" did not indicate any urgency in the danger, as there is no scientific proof of the adverse effects associated with comfrey. Although lack of scientific proof of health hazards makes withdrawal a viable option, RBVC may nevertheless prefer a recall in order to protect itself against potential consumer claims. By contrast, JOINTZ, which contains an allergen shellfish, will most likely have to be recalled without the option of withdrawal.

Conducting a Recall

Until the Food Safety Modernization Act of 2011 (FSMA), FDA did not have the authority to order a product recall; FDA may, however, request that firms conduct recalls. Even after FSMA, it should be expected that manufacturers will voluntarily carry out most recalls in accordance with recall guidelines set up by FDA, to be implemented through recall coordinators in each FDA district office. As in the case of JOINTZ, a company may discover on its own that one of its products presents a serious health risk (here, an undisclosed allergen risk due to a formulation error). The company may then take the initiative to recall the product, notify FDA of the recall, and abide by FDA recall guidelines. In other instances, FDA may be the one to discover a defect and request a recall. FDA may also alert a company to concerns requiring a recall that come to light during an inspection (e.g. failure to comply with Good Manufacturing Practices). In such cases, companies generally comply with the request.

Once FDA is involved in a recall, the agency will advise the company of the classification it has assigned to the matter based on the level of danger associated with the product and the potential health risk involved. A Class I recall involves products that can predictably cause serious health problems. Class II recalls involve products that might pose temporary health problems. Class III recalls involve products that are unlikely to cause health

problems but nevertheless violate FDA regulations. Class I recalls will always involve notifications to customers and distribution of a press release advising of an “urgent product recall” in order to communicate the urgency of the danger.

FDA generally encourages companies to advise it of all product recalls and expects regular progress reports. The agency will monitor the adequacy of the recalling company’s actions. After the recall, FDA investigates the source of the defect and ensures that the product is suitably destroyed or disposed of. FDA also expects the company to investigate and adopt corrective measures (e.g., new vendors, new standard operating procedures). This process will almost always involve an inspection of all facilities involved in the production of the recalled product.

An appropriate recall strategy must take into consideration the severity of the health hazards, the ease of identifying the product, the extent to which the defect is obvious to the consumer, the degree to which the product remains unused in the marketplace, and the continued availability of essential products. In addition, a recall strategy must assess the appropriate depth of the recall, whether or not to issue a public warning, and the extent of effectiveness checks. The depth of the recall involves the extent to which the recall will penetrate the distribution chain (consumer, retail, or wholesale). Depending on the health hazards and the extent of distribution, a recall may only need to reach wholesalers; a more extensive recall would reach the consumer level. Here, RBVC can probably limit withdrawal of REBOUND to distributors, whereas the recall of JOINTZ will need to reach the consumer level due to its serious health implications.

A recalling firm must notify each of its direct accounts of the recall. Such notice is subject to FDA review and must inform direct accounts that distribution of the product must cease and provide instructions regarding the disposal or return of the product. Where appropriate, the notice will also ask direct accounts to notify their consumers of the recall. Once the recall has been implemented, the recalling firm is responsible for producing periodic recall-status reports to the recall coordinator at the appropriate FDA district office so that the agency can monitor the progress of the recall. Reporting intervals are generally between two and



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299 Broadway Suite 1700
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four weeks but will ultimately depend on the urgency of the recall as determined by FDA. Progress reports should indicate the number of consignees notified of the recall, the number of consignees that responded (or did not respond to the recall), the date and method of notification, the amount of product involved, the number and results of effectiveness checks, and an estimated time frame for completion of the recall.

A recall will be terminated after FDA has determined that all reasonable efforts have been taken to remove or correct the product in accordance with the recall strategy and that there has been proper disposition of the product. A firm may also request termination of its recall if all the criteria have been met. The method of disposition of recalled product would depend on the type of defect. If, for example, a product was mislabeled, the company may re-package or sticker the product. If, however, the defect is an inherent danger, such as the product JOINTZ, destruction of the product will be more appropriate. Destruction of recalled product must be environmentally sound and must comply with EPA regulations. FDA will usually be satisfied with proof of proper disposal, but may, in certain circumstances, choose to witness destruction.

Recalls and FSMA

Before FSMA, if a company refused to comply with the recall request, FDA could only seek a court order to authorize a federal government seizure of the product. Now, however, FDA may issue an order requiring the responsible party to immediately cease distribution and notify other persons to immediately cease distribution of the food. Notification must be given to: (a) all persons manufacturing, processing, packing, transporting, distributing, receiving, holding, or importing and selling the food; and (b) all persons to which the food has been distributed, transported, or sold.

FDA must offer the responsible party the opportunity to an “informal” hearing to determine whether “adequate grounds” exist to continue the order to cease distribution within 48 hours after the order is issued. If, following the opportunity for a hearing, FDA determines that removal of the food from the market is necessary, the agency may order a recall or other appropriate action. FDA can then establish

timetables and require notice to consumers (publication of press releases in a manner likely to alert consumers) and periodic status reports. Failure to comply with a recall order is a prohibited act, subject to injunction, imposition of a civil fine, and/or criminal prosecution.

Conclusion

Although a recall may seem daunting to a company in the short term, with a proper understanding of the process and the assistance of counsel, the process can ultimately be beneficial. Failing to initiate a recall may lead to risks of product liability as well as long-term damage to a company’s reputation. More importantly, recalls also minimize the risk of harm to the public. Failure to take these factors into consideration greatly increases the likelihood that a company’s reputation will be severely damaged in the long term. In the cases discussed above, each of the recalls concluded with no apparent harm.

* * *

Marc Ullman is a partner at Ullman, Shapiro & Ullman in New York. He can be reached at 212.571.0068 or via [email](mailto:marc@usulaw.com).

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



IASC Files Complaint Citing Trademark Infringement of Certification Seal

The International Aloe Science Council (IASC), the global nonprofit trade organization representing the aloe vera industry, on August 12 filed a complaint in U.S. District Court for the District of Maryland against Fruit of the Earth (FOTE), based in Ft. Worth, Texas, for trademark infringement due to that company’s unauthorized use of the IASC Certification Seal.

According to the IASC's filing, FOTE's products were decertified at the beginning of 2011 after the company failed to provide samples for analytical testing. As per the program's policies and operations procedures, FOTE was to have immediately removed the seal from all products and marketing materials upon decertification.

"We received several inquiries from consumers who were considering purchasing or had already purchased Fruit of the Earth products in national retail outlets," said Devon Powell, executive director of IASC. "They were concerned when they found FOTE's products on IASC's 'No Longer Certified' list on the association's website and had contacted us directly for more information."

Powell noted that several attempts were made to communicate with FOTE directly to get the company to recall the products displaying the seal in the marketplace, including the issuance of several cease and desist letters. But IASC's efforts were ultimately unsuccessful, Powell said.

"Though it's regrettable that we have to litigate this issue, we have a responsibility to our program participants as well as to consumers interested in purchasing the highest-quality aloe vera products to ensure that the sanctity of the seal remains intact," he said. "It's obvious the seal is of value to consumers, and that is why we have on the website lists of currently certified and no-longer-certified products, as well as a list of manufacturers known to have displayed the seal without authorization."

IASC has maintained its third-party program, which certifies the content and purity of aloe vera in products, since the early 1980s. IASC authorizes the display of the program's trademarked seal to aloe vera product manufacturers and facilities that have passed a rigorous set of requirements that can include formula and label review for compliance with IASC and federal, state, and local laws, as well as analytical testing of products and raw materials. The program also involves random off-the-shelf testing of products to ensure ongoing compliance.



IASC Initiates Market Survey

As noted in the [IASC Update from May 23](#), Council officials met with Food and Drug (FDA) personnel on May 10, 2011, to discuss follow-up studies to the National Toxicology Program (NTP) two-year oral consumption study (in which the agency indicated it would be co-principle investigators with NTP) and related issues. As noted in the Update, a marketplace survey was to be undertaken to clearly demonstrate an understanding for what aloe vera ingredients can primarily be found in products that are prevalent in the marketplace (inner leaf, purified leaf, mixtures).

"The IASC will be conducting a market survey of raw material suppliers initially, and possibly finished-product suppliers later, to identify the primary ingredients used in the U.S. marketplace and in aloe vera products for oral consumption, currently believed to be decolorized inner-leaf juice, decolorized or purified whole-leaf juice, and non-decolorized inner-leaf juice," said IASC Executive Director Devon Powell. "FDA made it clear that the aloe vera industry needs to identify and characterize the ingredients in the marketplace definitively, and this market survey will assist in our ability to do that."

The results of the survey will be provided to FDA to better assist the agency in understanding the ingredients currently available in the marketplace and to reduce confusion.

IASC members who supply or grow raw materials for sale or use in finished products are asked to complete the survey and return the results to IASC promptly. Survey data will be kept confidential, and any reports to be made publically available or submitted to any government agency will have all corporate or proprietary information redacted.

The survey is [now available on the IASC website](#) (click link to download) and members with questions are encouraged to contact IASC.

Insurance Program Covers Prop. 65 and Label Claims Advertising, and Data-Security Breaches

A unique new liability insurance program that for the first time responds to California Proposition 65 claims is now available to International Aloe Science Council members and other companies in the dietary supplement trade.

The ThinkRisk Vitamin & Supplement (V&S) Program, part of ThinkRisk's Converging Risk Liability Policy, also provides coverage for false advertising and other similar claims, including labeling claims. Additionally, coverage is provided for media and intellectual property claims, such as trademark and copyright infringement, as well as for the consequences of a breach of data security.

Available through longtime American Herbal Products Association (AHPA) member Grifcon Enterprises and Dick Griffin, who has served as the manager of AHPA's longstanding liability insurance program for more than 15 years, the V&S Program was specifically created to benefit companies in the dietary supplement marketplace.

"AHPA worked very closely with ThinkRisk and Grifcon Enterprises on the Proposition 65 component of this program to develop a comprehensive and important offering of risk coverage that has not been previously available to dietary supplement companies," said Michael McGuffin, AHPA president. "In light of the highly expensive litigation costs that we've seen for companies to respond to Proposition 65 claims—often exceeding \$100,000 per settlement—this new V&S Program is a prudent form of protection for AHPA members."

This highly flexible policy provides businesses with protection in a number of key areas where digital-age businesses now do business—and which are often not covered in traditional commercial general-liability coverage. Participants in this program will also have access to risk-management material to mitigate their exposure to claims in these areas.

Specifically, the new V&S Program includes coverage for:

- Claims brought under California's Proposition 65, including defense expenses; attorneys' fees; and



The advertisement graphic features a green background with the word "Aloe" in a large, stylized, yellow-to-green gradient font at the top. Below it, the text "BIO Natural & Sustainable Purity" is written in a similar gradient font. In the center, there is a circular image of an Aloe Vera plant in a field, with a person wearing a mask and gloves working nearby. The image is framed by a green recycling symbol. At the bottom of the graphic, there is contact information for Aloe Vera JAUMAVE, including a phone number, fax number, email address, and website URL.

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- First-party and third-party costs arising out of a breach of data security, including notification costs, data restoration, crisis management, credit monitoring, cyber investigation, cyber extortion, and civil fines and penalties.

This new coverage is backed by the financial strength of Great American Insurance Group and is rated “A” (Excellent) by A.M. Best as of the most recent rating evaluation dated May 10, 2010.

For more information on this innovative liability insurance program and to evaluate how the coverage can address your company’s insurance needs, contact Dick Griffin, Grifcon Enterprises, via phone: 916.434.8874 or email, or visit the firm’s [website](#).

As an additional resource, in 2010, AHPA created a “Primer on Products Liability Insurance for the Dietary Supplement Industry,” to provide a basic understanding of products liability insurance and the processes involved in purchasing this insurance by dietary supplement companies. This document is organized in a question and answer format and addresses numerous issues that are commonly encountered in obtaining products liability insurance. Click [here](#) to download the AHPA insurance primer.

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A HACCP Primer for Foods and Ingredient Suppliers

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

What is Hazard Analysis and Critical Control Point (HACCP)? Did it come from outer space? Has it been adopted by a world government? And if so, so what? Will it make our food supply safer?

The Food Safety Modernization Act (FSMA) was signed into law January 4, 2011. The law mandates “hazard analysis and risk-based preventive controls” in the processing and manufacture of food, including ingredients for use in dietary supplements. This is the term Congress used, and it is based on the HACCP concepts that have been followed by many in the food industry for years and which are imposed by the Food and Drug Administration (FDA) and U.S. Department of Agriculture regulations for particular foods.

The equivalent of HACCP will be in place for all foods under FSMA and will impact all International Aloe Science Council members who are ingredient suppliers and subject to food regulation. Dietary supplement manufacturers will continue to be subject to cGMP requirements for supplements.

What is HACCP, where did it come from, and who follows it? Below is an explanation from FDA Deputy Commissioner for Foods Michael Taylor from a speech given at George Washington University on May 19, 2011:

It (HACCP) is . . . the approach to food safety that the food industry pioneered in the early 1960s, originally to guarantee as much as possible the safety of food for space flights. Needless to say, reacting to food-safety problems while orbiting the Earth is not a good strategy, so food-industry experts developed a system known as Hazard Analysis and Critical Control Point

Systems – HACCP – to build prevention into the processing of the food.

HACCP is very much in line with good public-health practice. It focuses systematically on:

- *Understanding the specific food-safety hazards that could affect a particular food-production operation*
- *Devising and implementing scientifically validated controls to minimize the hazards*
- *Monitoring the implementation of preventive controls to verify effectiveness, and*
- *Making corrections and adjustments as needed, based on experience.*

Many food processors implement HACCP today as part of their own food-safety and quality-assurance systems, and, with industry support, HACCP approaches have been implemented by FDA and USDA as a regulatory standard for low-acid canned food, seafood, juice, meat, and poultry. HACCP is also an internationally recognized framework for food safety, through its adoption by the United Nations Codex Alimentarius Commission and other national governments. HACCP-based prevention is thus already recognized as the operating principle and standard for food safety by much of the food industry.

Think about HACCP and its importance to food safety as the European Union struggles to find the cause of the current E. coli outbreak that has been associated with 44 deaths at the time of this publication.

Michael Taylor's complete speech can be found [here](#).

The American Herbal Products Association (AHPA) will alert members as FDA develops the concepts for hazard analysis and risk-based preventative controls for food.

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The Food Safety Modernization Act: A Review of Implementation Meetings and Strategies

by Merle Zimmermann, Ph.D., AHPA Information Analyst

The [Food Safety Modernization Act \(FSMA\)](#), passed by Congress in December 2010 and signed by President Obama in January 2011, has revolutionized the field of food safety. The biggest change to food safety law since the passage of the Federal Food, Drug, and Cosmetic Act in 1938, the FSMA provides the Food and Drug Administration (FDA) with extended powers in its mission of protecting the nation's food supply and also enacts a paradigm shift in the agency's approach to food safety.

Instead of FDA having to primarily *react* to individual food-hazard events, FDA is now able to be *proactive* and prevent such events from occurring at all. The new law tasks the agency and industry to apply science-based hazard analysis and preemptive auditing to identify and isolate questionable goods before they are released to the marketplace. Among other provisions, the FSMA places additional responsibilities on importers for the safety of their food products and provides FDA with the power to detain said products when agency agents have "reason to believe" the products are adulterated or misbranded.

While the FSMA is focused primarily on food production and products, the law is of importance to dietary supplement manufacturers and suppliers because elements of it apply to individual ingredients and facilities both inside and outside the United States. Exemptions exist to parts of the law applying to dietary supplement manufacturers, and these exemptions are equally applicable to both domestic and foreign firms due to U.S. trade agreements. (See the *AHPA Updates* of [Dec. 20, 2010](#), and [April 15, 2011](#), for further discussion of this topic.)

FDA held several public meetings and hearings in March, April, and June 2011 to present and discuss how FDA should implement certain sections of the FSMA. In addition, FDA introduced a [FSMA web portal](#) focused on the new law. New rules resulting from FSMA will apply to all food sold in the United States, including imported food.

During all of the proceedings, FDA staff underscored the common goal of food safety being shared by government regulation, industry, and consumers, and how the development of the FSMA would be a cooperative journey with government and industry working together.

After the law's passage, I attended the public FDA events, collecting information and comments on the FSMA throughout the proceedings. Aside from overview speeches discussing the entire law, three major topic groups were covered in five FDA meetings, hearings, and media briefings over the last four months.

The FSMA and Importing Activities

The focus of the first two meetings was on the pending implementation of some of the elements of FSMA Title III, *Improving the Safety of Imported Food*. More specifically, the March 29 meeting was titled, "[FSMA and Imports: A New Paradigm for Importers](#)," and focused on the changes directly affecting FDA and

interested parties such as growers, manufacturers, importers, and auditors. The March 30-31 meeting was called "[Ensuring the Safety of Imported Foods and Animal Feed: Comparability of Food Safety Systems and Import Practices](#)" and focused more on inter-government, bank, and multinational infrastructure development as opposed to individual comments.

The first two meetings covered the same topics, however, and provided FDA ample opportunity to discuss the following sections of the FSMA in detail:

- Foreign Supplier Verification Program (Section 301)
- Voluntary Qualified Importer Program (Section 302)
- Building Capacity of Foreign Governments (Section 305)
- Accreditation of 3rd-Party Auditors (Section 307)

During these meetings, FDA staff repeatedly stressed the risk-management nature of the new law, which requires

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FDA to efficiently use its resources and to focus testing and regulation efforts on high-risk foods and food ingredients while continuing to monitor low-risk products at a lower rate. Participation in the agency's voluntary supplier-verification and qualified-importer programs were suggested as ways that responsible companies could demonstrate their reduced levels of risk. FDA stated that participation in the programs would not necessarily put shipments in an express lane through the border, however.

The agency also recognized that U.S. trade obligations require both domestic and foreign producers and importers to be treated on an equal footing. It communicated its understanding of the potential impact of new costs on small businesses and stated its intention to minimize these while still meeting its food safety goals.

FDA promised that any new importer requirements would be clearly and widely publicized well in advance of compliance dates.

Representatives from FDA explained that the last section, Accreditation of 3rd-Party Auditors (Section 307), will require accredited auditors to notify FDA of conditions that "could cause or contribute to a serious risk to the public health" during both regulatory and consultative audits and welcomed further comments and suggestions to clarify the exact scope of this section of the law.

In a recent media briefing on international drug and food issues conducted by FDA, on June 20, 2011, these points were revisited. FDA emphasized its commitment to international interagency cooperation and communication in implementing this part of the new law and the importance of the third-party auditing program in vetting imports and facilities for compliance. FDA mentioned that, in some cases, third-party auditing certification might be essential for products to be straightforwardly imported across the border.

The agency is encouraging a position where the border crossing would primarily serve as a checkpoint where prior data would be reviewed and approved by the agency as opposed to its current, more elaborate role.

The FSMA and Preventative Controls

On April 20, 2011, FDA continued its outreach program on the FSMA law by holding a meeting

entitled, "[Focus on Preventative Controls for Facilities.](#)"

The focus of this meeting in the ongoing series was on preventative controls used by facilities to identify and address hazards associated with specific foods and food processes.

The FSMA sections of particular interest in this meeting included:

- Inspections of Records (Section 101)
- Hazard Analysis and Risk-based Preventative Controls (Section 103)
- Performance Standards (Section 104)

Discussion primarily centered on Section 103, Hazard Analysis and Risk-based Preventative Controls.

Hazard analysis was discussed in the framework of Hazard Analysis and Critical Control Points (HACCP), a process where identifying and controlling potential food-safety hazards becomes the focus of a manufacturing safety system. This approach to product quality originated during World War II and was utilized during the NASA space flight program, where after-production testing to verify quality of artillery shells and astronaut dietary meals was impractical. When applied to food manufacturing, HACCP plans provide a systematic, science-based method to ensure food safety. It also provides for a new type of inspectional auditing, as a manufacturing plant's HACCP plan can be reviewed and validated independently of physical inspection of the facility.

The U.S. Department of Agriculture has published a very clear, generic [HACCP guide](#) for processing plants preparing raw meat and poultry products which, though it is focused on a different industry, nevertheless provides good insight into applying the HACCP philosophy.

During a breakout session discussing preventative controls, FDA received a question from a webcast attendee regarding food categorization of high- and low-risk foods, and [asking for further clarification](#). Jenny Scott, senior advisor to the director of the Office of Food Safety at FDA's Center for Food Safety and Applied Nutrition, answered: "What is food

categorization? ... We were intentionally vague in what we said here because we were hoping you would tell us how you might categorize foods. One question: Is it high risk or not?" This theme of public participation flows throughout FDA's approach to the FSMA, with the agency welcoming information on how it should prioritize preparing best practices from existing companies and trade associations.

Codex Alimentarius standards were also mentioned as a possible source of guidance for FDA, which the agency accepted gratefully.

The definition of a facility was also discussed, as well as the distinction between what determines a large and small facility. Due to international trade agreements, all such definitions would apply equally to facilities stateside and overseas, and it was noted that exceptions related to "small" and "very small" businesses would need to be written carefully to be fair and equitable to both domestic and foreign producers. Although "small" businesses are limited to conducting operations within 275 miles from their headquarters or within the same state, the "very small" business category had no such restriction.

It was noted that some very large operations had 25 or fewer employees, due to efficiencies gained in automating their facilities. FDA stated that it would consider the suggestions carefully to ensure that small businesses were not unfairly burdened.

FDA suggested working with industry representatives to conduct safety and/or HACCP training for small businesses. The agency was interested in leveraging preexisting organizations and programs to distribute information.

Following further discussion, attendees requested that FDA issue clear and direct guidance documents on the new laws to make it easier for small businesses to educate themselves about compliance with new and upcoming regulations. When asked about a particular guidance, which did not yet exist, FDA staff stated that it would be added to the list of documents to be produced.

FDA representatives agreed on the importance of clear documentation and requested that comments be submitted to the FSMA dockets requesting any

guidances that are needed so that the agency could prepare them and avoid future confusion.

FSMA's Inspections and Compliance Provisions

On June 6, 2011, FDA engaged the community once more with a public meeting titled, "[FDA Food Safety Modernization Act: Focus on Inspections and Compliance Provisions](#)."

At the meeting, FDA provided a forum for interested persons to address the guidance, regulation, and/or the implementation activities related to the following topics:

- Enforcement Authorities
- Frequency and Targeting of Facility Inspections
- Manner of Inspection in a Preventative Controls Environment
- Enhancement of the Reportable Food Registry

Several key themes reappeared throughout the discussion.

During a discussion on how best to identify risk across the large variety of different manufacturing approaches and facilities, it was suggested by interested parties to conduct a joint FDA-industry study on well-blinded data from across the entire production process. Collected data could include results from a variety of different tests, biological and otherwise. The study might be a good way to identify high- and low-risk conditions in practical situations, providing concrete safety data across a wide spectrum of manufacturing methods.

FDA, however, expressed disinterest in participating, noting a potential conflict of interest that might arise if the agency handled the blinded, raw testing data: as the participants would be anonymous, if FDA became aware of a potential food-safety issue from the study data, the agency would be unable to fulfill its responsibilities to take regulatory action. Nevertheless, the agency agreed that the information garnered from such a study would be invaluable in a science-based determination of food risk and reacted positively to the idea that industry could conduct such studies independently and report bottom-line results to the agency, which could then use them to enhance its food safety activities under the FSMA.

Further discussion of how FDA would allocate its inspection resources for the greatest benefit focused on the need for FDA to develop a matrix-based approach that would allow investigators to consider the qualities of facilities and their operators along with the products they were involved in producing. Third-party auditing was suggested—along with food-risk assessment and HACCP-plan evaluation of manufacturing processes—as a means of deciding which facilities most needed inspection.

Attendees recommended FDA require all manufacturing operations to submit HACCP plans on request to avoid document management issues and an unfair burden to small operators who might not have dedicated HACCP officers.

Discussion at the meeting also touched on the additional powers given to FDA regarding product recalls and product holding. It was generally agreed that the FSMA, aside from granting the agency additional enforcement options, required it to use these extended enforcement powers in a responsible and clear fashion.

Some of those present requested that FDA issue a

guidance as soon as possible clearly explaining its uses of its new enforcement responsibilities and how they would fit into the current system of warnings and actions. It was also discussed that although FDA inspectors would initiate some of these new enforcement activities, the responsibility for any actions clearly needed to remain with commissioner-level agency personnel, as the law states.

Conclusion

The FSMA is clearly a game changer in the food safety field. The new focus on risk-analysis activities from FDA and its willingness to modify its point of view in response to comments from interested parties makes participating in these proceedings of high importance for industry.

The new law requires FDA to increase the frequency of inspections to at least once every five years for low-risk facilities and products, and once every three years for high-risk facilities and products.

The American Herbal Products Association (AHPA) already has guidances available to assist with [inspection](#)



The International Aloe Science Council

Presents an

Aloe Scientific Primer



[proceedings](#) and other essential topics. These are available in the [bookstore](#) on the AHPA website.

Further information on the three meetings held between FDA and industry is available. FDA has posted agendas and webcasts of the proceedings, available on-demand on the agency's website:

- [Importing and Foreign Inspection Provisions of FSMA, March 29, 2011](#)
- [Preventative Controls in FSMA, April 20, 2011](#)
- [Inspections and Compliance Provisions of FSMA, June 6, 2011](#)

FDA is continuing to accept general written comments on FSMA, and AHPA's Government Relations Committee is reviewing the process in the interim and plans to provide commentary. Please contact [Michael McGuffin](#) if you would like to participate in AHPA's review or would like to contribute to the comments.

* * *

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Guava Leaf Monograph

- ◆ Metwally AM, Omar AA, Ghazy NM, Harraz FM, El Sohafy SM. [Monograph of *Psidium guajava* L. leaves](#). *Phcog J*. 2011 April;3(21):89-104.

This monograph was developed to establish standards for guava leaves used medicinally. It is compiled in a classic pharmacognostic fashion with sections on nomenclature, history, identification, including macroscopic, microscopic, and thin-layer chromatography (TLC) descriptions—the TLC image mentioned is unfortunately missing—constituents, about 20 pharmacological actions, toxicity, and an assay for quercetin content. Different ratios of ethanol and water for infusions and decoctions were examined to maximize extraction efficiency based on quercetin as a marker compound.

FDA Collaborative Validation of Pesticide-Residue Analysis

- ◆ Sack C, Smoker M, Chamkasem N, Thompson R, Satterfield G, Masse C, Mercer G, Neuhaus B, Cassias I, Chang E, Lin Y, Macmahon S, Wong J, Zhang K, Smith RE. [Collaborative validation of the QuEChERS procedure for the determination of pesticides in food by LC-MS/MS](#). *J Agric Food Chem*. 2011 June 22;59(12):6383–6411.

Seven FDA laboratories collaborated to validate the QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) extraction procedure combined with HPLC-MS/MS analysis to detect, identify, and confirm the identity of 173 pesticides in carrot, spinach, and orange matrices in less than 20 minutes. Most of the compounds (161 of 173) could be detected at less than 10 ng/g (10 ppb) concentration levels. The procedure was shown to be specific, accurate, reproducible, sensitive, and linear as an effective screening tool for the determination of pesticide residues in these materials.

FDA Finds Pesticides Must be 5-10 ppb to Consistently Measure

- ◆ Zhang K, Wong JW, Yang P, Tech K, Dibenedetto AL, Lee NS, Hayward DG, Makovi CM, Krynitsky AJ, Banerjee K, Jao L, Dasgupta S, Smoker MS, Simonds R, Schreiber A. [Multiresidue pesticide analysis of agricultural commodities using acetonitrile salt-out extraction, dispersive solid-phase sample clean-up, and high-performance liquid chromatography-tandem mass spectrometry](#). *J Agric Food Chem*. 2011 Jun 14. doi: 10.1021/jf2010723 [Epub ahead of print]

This larger study evaluated matrix effects for 209 pesticides in apple, avocado, beet, bell pepper, blueberry, broccoli, cabbage, carrot, corn, cucumber, eggplant, grape, green bean, onion, orange, peach, potato, spinach, strawberry, tomato, ground hazelnuts, honey, milled wheat flour, and raisins again using QuEChERS extraction and HPLC-MS/MS analysis. The researchers concluded that analytes must have concentrations of at least 5-10 ppb to obtain consistent results using their methodology. They demonstrated fitness for screening

and surveillance applications of the methods with pesticide concentrations ranging from 2.5 to >1000 ppb in a variety of agricultural samples.

Using Genetics and Chemistry to Determine Natural Product Origin

- ◆ Wen H, Lee MY, Song Y, Moon S, Park S. [Combined genomic-metabolomic approach for the differentiation of geographical origins of natural products: Deer antlers as an example.](#) *J Agric Food Chem.* 2011 June 22;59(12):6339–6345.

Although deer antlers were the example used in this study of determining the geographical origin of a natural product, the lesson may also apply to herbs. This is particularly true where more than one species may be involved. If different species are limited to different growing regions, then DNA analysis may provide genomic data sufficient to pinpoint where each item was grown. However, when the same species are grown in different countries and regions, as can happen with botanicals, then an additional analysis of the plant's metabolites, a metabolomic study, can provide the key to their origin.

Using a sufficient number of samples from Canadian, Korean, and New Zealand locations, these researchers were able to determine the origin of deer antler samples by first separating them into species by their DNA and then further by their chemistry based on NMR spectral data. The authors state their belief that this method is “generally applicable to many herbal medicinal products for which various species are grown internationally.”

The Beginning of the End of ORAC Marketing?

- ◆ Finley JW, Kong AN, Hintze KJ, Jeffery EH, Ji LL, Lei XG. [Antioxidants in foods: State of the science important to the food industry.](#) *J Agric Food Chem.* 2011 Jun 10. doi: 10.1021/jf2013875 [Epub ahead of print]

This paper supports the one by Hollman et al., reported on previously, that was not able to conclude that measures of antioxidant activity correlate with direct health benefits and which calls into question

the concept that health benefits are derived from antioxidant-rich materials through direct action of high oxygen radical absorbance capacity (ORAC) values acting to directly quench reactive oxygen species (ROS) in the body. Recent findings indicate that antioxidant function may also affect gene expression that produces antioxidant enzymes. Several other mechanisms by which antioxidant function may be regulated are also explored in this review, including recent evidence suggesting that low levels of ROS may be needed to stimulate an antioxidant response from the body, and it may be detrimental to remove too many of them.

The authors point out that ORAC tests used to promote polyphenol-rich products measure only direct-acting ROS quenching and because they reach only low levels in plasma after ingestion “may play a very minor role in antioxidant balance.” It is clear that the understanding of the “health roles of antioxidants is changing and nutritional messages used to market antioxidant-containing foods often are not supported by contemporary evidence,” they add. The authors also point out that recent findings have “implications for the fortification of foods with antioxidants, as well as for the consumption of many dietary supplements” and the corollary “that supplemental doses of some antioxidants may block beneficial actions of other physiological processes, and at high doses some antioxidants may be toxic.”

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- ◆ [Unlocking Aloe Vera's Healing Secrets](#) – ABC News, Technology
- ◆ [NTP Speaks about Aloe Vera](#) – NIEHS (National Institute of Environmental Health Sciences)

- ◆ [New Report Just Published: Nutraceuticals: Global Markets and Processing Technologies](#)
– Reportlinker
- ◆ [Transdermal Delivery; Research from University of Halle Provide New Insights into Transdermal Delivery](#)
– Obesity, Fitness & Wellness Week
- ◆ [Processing, Food Applications and Safety of Aloe Vera Products: A Review](#) –
Journal of Food Science and Technology, 48, 5 (Oct. 2011): 525-533
- ◆ [Solids Handling: Spray Drying Smooths Aloe Vera Process](#) – GEA Niro
- ◆ [Aloe Vera Gel Antioxidant with Cholinergic Innervations](#) – Saarbrücken VDM Verlag Dr. Müller
- ◆ [Aloe \(aloe Vera\): Monograph](#) – Mayo Clinic
- ◆ [World First for Aloe Vera Farm](#) – Newsmail
- ◆ [Aloe Vera Puts a Stop to Irritable Bowel Syndrome](#) – Online PR Media
- ◆ [Warning Flag Raised over Aloe Vera](#) – World News, Australia



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The image shows a large field of green Aloe Vera plants under a blue sky. Overlaid on the right side is a circular seal with a serrated edge. The seal features a central Aloe Vera leaf icon and the text 'ALOE GUARANTEE & PURITY IN THE PRODUCT' at the top, 'INTERNATIONAL ALOE SCIENCE COUNCIL' at the bottom, and 'CERTIFIED' in large letters across the middle.



LEGAL & LEGISLATIVE NEWS

Sens. Durbin and Blumenthal Introduce Dietary Supplement Legislation in the Senate

Sens. Dick Durbin, D-Ill., and Richard Blumenthal, D-Conn., on June 30 introduced legislation that, according to a [press release](#) posted on Durbin's website, "would ensure that consumers have the information they need to distinguish between products that are safe and others that contain potentially dangerous ingredients which haven't been approved by the Food and Drug Administration (FDA).

"The Dietary Supplement Labeling Act would improve the information available to consumers, and to curb the prevalence of drinks and foods that are masquerading as dietary supplements as a means of avoiding reviews and regulation by the FDA," according to Durbin in the release.

According an earlier [press release](#) posted on Durbin's site on June 27, the bill would:

- Direct the Food and Drug Administration (FDA) to establish a definition for "conventional foods."
- Require supplement labels to disclose known risks of ingredients and to display a mandatory warning if the product contains a dietary ingredient that may cause potentially serious adverse events.
- Require manufacturers to register dietary supplement products with FDA, and provide a description of each dietary supplement, a list of ingredients, and a copy of the label.
- Require supplement labels to include a batch number.

Durbin's June 27 press release makes it clear that he is most focused on products in food or beverage forms and specifically mentions several liquid brands, including Rockstar Energy Drink, 5-Hour Energy, and Drank. The latter contains melatonin and, according to the press release, the company rebranded the product as

a dietary supplement when FDA issued a warning letter last year, which identified melatonin as an unapproved food additive. According to Durbin, "FDA has not yet taken action, because without a clear definition for 'conventional food and beverage' it is difficult to address this kind of conflict."

"In reviewing this press release, it appears that this bill would largely propose legislative solutions where what is needed is regulatory enforcement," commented Michael McGuffin, president of the American Herbal Products Association (AHPA). "Supplements may not be represented as conventional foods and must be labeled to include all information—including safety information—that is material in light of the consequences that may result from their use. And while no one will argue with the wisdom of using product lot numbers, it is already the standard industry practice to do so."

The most controversial part of the Dietary Supplement Labeling Act may well be its requirement for product registration, a change that Durbin has sought in the past.

"AHPA is in communication with Senator Durbin's office, and I will be reviewing the actual legislation as soon as it is available," added McGuffin. "As always, AHPA's primary focus will be on identifying and opposing any legislation that in any way reduces consumer access to safe dietary supplements."

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Consent-Decree Conviction and Dividing Up Ill-Gotten Gains

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

Signing a consent decree is serious business.

Once a consent decree, a judicial decree that sanctions a voluntary agreement between parties in a dispute, has been signed and is in force, it must be complied with.

When a company is found to be out of compliance or evading it, the consequences can be substantial.

Quality Formulation Laboratories, American Sports Nutrition, and the companies' owner and managers were each found guilty of [criminal contempt](#) in violating a consent decree regarding the operation of their dietary supplement manufacturing businesses. The consent decree required that the defendants shut down their manufacturing operations and not reopen their current facilities or any other ones without first correcting these violations and getting the Food and Drug Administration's (FDA) approval to reopen.

The criminal contempt charges alleged that managers Ahmad Desoky and Omar Desoky, with knowledge of the court's order, assisted their father, company owner Mohamed S. Desoky, in violating the order, and thus were criminally liable for the violations, even though they were not named as defendants in the original civil case.

What did they do? They set up their businesses in a separate location in another state, almost immediately after signing the consent decree. They moved their employees and their equipment to the new location. And they operated their former New Jersey facility in violation, as well.

They were convicted on the criminal contempt charges in a jury trial and at press time await sentencing. Really, are the cGMPs for dietary supplements that difficult to meet?

Where Does All That Forfeiture Money Go?

It's increasingly true that crime doesn't pay. In successfully prosecuted criminal cases, the "fruits" of any crime are seized, whether those fruits are in bank accounts or in material assets such as big houses, cars, or boats. For example, the Federal Trade Commission (FTC) takes seized fruits and sets up a system to try to return illegally gotten funds back to consumers who were misled.

In the CortiSlim weight-loss dietary supplement case against Window Rock Enterprises Inc. and Infinity Advertising Inc., Los Angeles-based companies that sold the product, FTC took two of the guilty parties' homes, a boat, a car, and the title to one of the defendant's relative's home (while allowing the relative

to live in it while they remained alive).

In the [Genescience Pharmaceuticals](#) case, where a Chinese drug company and its CEO were found guilty for illegally marketing human growth hormone in the United States, \$4.5 million was divided up among law enforcement offices in Rhode Island, and the defendants were required to donate \$3 million to the Rhode Island Foundation to support sports anti-doping efforts.

The company had previously forfeited an additional \$2.7 million in the case.

"I am pleased that this ground-breaking federal prosecution, which was a success on so many levels, has resulted in the distribution of such significant, forfeited amounts to state and local law enforcement agencies in Rhode Island. The defendants paid directly for their misconduct through the forfeiture of these assets," noted U.S. Attorney Peter F. Neronha.

Successful law enforcement is a growing vehicle for financing prosecutors and police forces. In California, county district attorneys' offices use the money they receive from consumer-protection-case awards or settlements to fund their offices. And in many states, weights and measures enforcers do the same. In states along the Florida–New York corridor, law enforcement is funded by the value of seized drugs, cash, and cigarettes.

* * *

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[Invitro screening for biological and pharmacological effects of indigenous medicinal plants, mentha longifolia and aloe vera](#)

Abstract

The crude ethanolic extracts of *Mentha longifolia* Linn. (leaves and stem) and *Aloe vera* (leaves) were screened for various *invitro* biological and phannacological activities including antifungal, antibacterial,

insecticidal, phytotoxic activities, and brine-shrimp lethality. All the extracts exhibited remarkable (~60%) phytotoxic activity in the highest tested concentration (500 ppm) against *Lemna minor* L. with *Aloe vera* extract showing complete inhibition of the studied plant. The *Mentha longifolia* Linn. (stem) and *Aloe vera* extracts were also explored to possess good (~55%) antifungal activities against *Trichophyton longifusus*, (75% and 60%), and *Microsporum canis* (65% and 55%), respectively, while *Mentha longifolia* Linn. (leaves) displayed only a weak (~50%) activity against *Trichophyton longifusus* and *Fusarium solani* (20% each). These extracts were found to be devoid of any antibacterial, insecticidal activities and brine-shrimp lethality during this study.

Interventions for preventing oral mucositis for patients with cancer receiving treatment (Review)

Abstract

BACKGROUND: Treatment of cancer is increasingly more effective but is associated with short- and long-term side effects. Oral side effects remain a major source of illness despite the use of a variety of agents to prevent them. One of these side effects is oral mucositis (mouth ulcers).

OBJECTIVES: To evaluate the effectiveness of prophylactic agents for oral mucositis in patients with cancer receiving treatment, compared with other potentially active interventions, placebo, or no treatment.

METHODS: Electronic searches of Cochrane Oral Health Group and PaPaS Trials Registers (to 16 February 2011), CENTRAL (*The Cochrane Library* 2011, Issue 1), MEDLINE via OVID (1950 to 16 February 2011), EMBASE via OVID (1980 to 16 February 2011), CINAHL via EBSCO (1980 to 16 February 2011), CANCERLIT via PubMed (1950 to 16 February 2011), Open SINGLE (1980 to 2005) and LILACS via the Virtual Health Library (1980 to 16 February 2011) were undertaken. Reference lists from relevant articles were searched and the authors of eligible trials were contacted to identify trials and obtain additional information.

SELECTION CRITERIA: Randomised controlled

trials of interventions to prevent oral mucositis in patients receiving treatment for cancer.

DATA COLLECTION AND ANALYSIS: Information regarding methods, participants, interventions, outcome measures, results, and risk of bias were independently extracted, in duplicate, by two review authors. Authors were contacted for further details where these were unclear. The Cochrane Collaboration statistical guidelines were followed and risk ratios calculated using random-effects models.

Interventions for treating oral lichen planus

Abstract

BACKGROUND: Oral lichen planus (OLP) is a common chronic autoimmune disease associated with cell-mediated immunological dysfunction. Symptomatic OLP is painful and complete healing is rare.

OBJECTIVES: To assess the effectiveness and safety of any form of therapy for symptomatic OLP.

SEARCH STRATEGY: The following electronic databases were searched: the Cochrane Oral Health Group Trials Register (to 26 January 2011), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 1), MEDLINE via OVID (1950 to 26 January 2011) and EMBASE via OVID (1980 to 26 January 2011). There were no restrictions regarding language or date of publication.

SELECTION CRITERIA: All randomised controlled clinical trials (RCTs) of therapy for symptomatic OLP, which compared treatment with a placebo or between treatments, or no intervention were considered in this review.

DATA COLLECTION AND ANALYSIS: The titles and abstracts of all reports identified were scanned independently by two review authors. All studies meeting the inclusion criteria were assessed for risk of bias and data were extracted. For dichotomous outcomes, the estimates of effects of an intervention were expressed as risk ratios (RR) together with 95% confidence intervals. For continuous outcomes, mean differences (MD) and 95% confidence intervals were used to summarise the data for each group. The statistical unit was the patient. Meta-analyses

were done only with studies of similar comparisons reporting the same outcome measures.

MAIN RESULTS: 28 trials were included in this review. Pain is the primary outcome of this review because it is the indication for treatment of OLP, and therefore this review indicates as effective, only those treatments which significantly reduce pain. Although topical steroids are considered first line treatment for symptomatic OLP, we identified no RCTs that compared steroids with placebo. There is no evidence from the three trials of pimecrolimus that this treatment is better than placebo in reducing pain from OLP. There is weak evidence from two trials, at unclear and high risk of bias respectively, that aloe vera may be associated with a reduction in pain compared to placebo, but it was not possible to pool the pain data from these trials. There is weak and unreliable evidence from two small trials, at high risk of bias, that cyclosporin may reduce pain and clinical signs of OLP, but meta-analysis of these trials was not possible. There were five trials that compared steroids with calcineurin inhibitors, each evaluating a different pair of interventions. There is no evidence from these

trials that there is a difference between treatment with steroids compared to calcineurin inhibitors with regard to reducing pain associated with OLP. From six trials there is no evidence that any specific steroid therapy is more or less effective at reducing pain compared to another type or dose of steroid.

AUTHORS' CONCLUSIONS: Although topical steroids are considered to be first line treatment, we identified no RCTs that compared steroids with placebo in patients with symptomatic OLP. From the trials in this review there is no evidence that one steroid is any more effective than another. There is weak evidence that aloe vera may reduce the pain of OLP and improve the clinical signs of disease compared to placebo. There is weak and unreliable evidence that cyclosporin may reduce pain and clinical signs of OLP. There is no evidence that other calcineurin inhibitors reduce pain compared to either steroids or placebo. From the 28 trials included in this systematic review, the wide range of interventions compared means there is insufficient evidence to support the effectiveness of any specific treatment as being superior.

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Inhibitory effect of botanical extracts against *Alternaria alternata* of aloe vera dry rot

Abstract

Aloe vera dry rot caused by *Alternaria alternata*, is one of the most serious fungal diseases affecting the commercial cultivation of aloe vera in North India. Control of this disease through chemical is quite expensive and not ecofriendly. The plant extracts as biopesticides act as a vital components for the management of this disease. Evaluation of some plant extracts was carried out against *A. alternata* in laboratory conditions. The extracts were prepared at 5% and 10% concentration and were evaluated through inhibition in radial growth (food poison technique) and spores (conidia) germination (hanging drop technique) against *A. alternata*. Neem leaf extract gave 58.6% inhibition in radial growth and 56.5% in spore germination at 10% concentration followed by Ocimum sanctum which was found effective and gave 54.7% inhibition in radial growth and 50.4% in spore germination over control.

In vitro effect of Aloe vera, Coriandrum sativum and Ricinus communis fractions on Leishmania infantum and on murine monocytic cells

Abstract

In South America, visceral leishmaniasis is a zoonosis caused by the protozoan species *Leishmania infantum* (syn. *L. chagasi*) and is primarily transmitted through the bite of the female *Lutzomyia longipalpis*. Its main reservoir in urban areas is the dog. The application of control measures recommended by health agencies have not achieved significant results in reducing the incidence of human cases, and the lack of effective drugs to treat dogs resulted in the prohibition of this course of action in Brazil. Therefore, it is necessary to search new alternatives for the treatment of canine and human visceral leishmaniasis. The objectives of this study were to evaluate the *in vitro* effect of fractions from *Aloe vera* (aloe), *Coriandrum sativum* (coriander), and *Ricinus communis* (castor) on promastigotes and amastigotes of *L. infantum* and to analyze the toxicity against the murine monocytic cells RAW 264.7. To determine the viability of these substances on 50% parasites (IC₅₀), we used a tetrazolium dye (MTT) colorimetric assay (bromide 3-(4,5-dimethylthiazol-2-yl)-2,5-dephenyltetrazolium),

and on amastigotes we performed an *in situ* ELISA. All fractions were effective against *L. infantum* promastigotes and did not differ from the positive control pentamidine ($p > 0.05$). However, the *R. communis* ethyl acetate and chloroform fractions, as well as the *C. sativum* methanol fraction, were the most effective against amastigotes and did not differ from the positive control amphotericin B ($p > 0.05$). The *R. communis* ethyl acetate fraction was the least toxic, presenting 83.5% viability of RAW 264.7 cells, which was similar to the results obtained with amphotericin B ($p > 0.05$). Based on these results, we intend to undertake *in vivo* studies with *R. communis* ethyl acetate fractions due the high effectiveness against amastigotes and promastigotes of *L. infantum* and the low cytotoxicity towards murine monocytic cells.

RESULTS: IC₅₀ values of ethyl acetate, chloroform, and methanol fractions of *A. vera*, *Coriandrum sativum*, and *R. communis* on promastigotes and amastigotes of *L. infantum* are summarized on [Table 1](#). Besides, the drug reference used in the *in vitro* tests on promastigotes was pentamidine and on amastigotes was amphotericin B. Briefly, all fractions were effective against *L. infantum* promastigotes and did not differ from the positive control pentamidine ($p > 0.05$). However, the *R. communis* ethyl acetate and chloroform fractions, as well as the *C. sativum* methanol fraction, were the most effective against amastigotes and did not differ from the positive control amphotericin B ($p > 0.05$).

Comparison of Treatment Efficacy of Daily Use of Aloe Vera Mouthwash With Triamcinolone Acetonide 0.1% on Oral Lichen Planus: A Randomized Double-Blinded Clinical Trial

Abstract

INTRODUCTION: Corticosteroids are the mainstay for treatment of oral lichen planus (OLP) and have their own side effects. The aim of this study was to compare the therapeutic effects of aloe vera (AV) mouthwash with triamcinolone acetonide 0.1% (TA) on OLP.

METHODS: A total of 46 patients with OLP were enrolled in this study. The patients were randomly divided into 2 groups. Each group was treated with received AV mouthwash or TA. The treatment period for both groups was 4 weeks. The basement data were recorded for each patient. Patients were evaluated on

days 8, 16, and after completing the course of treatment (visit 1-3). The last follow-up was 2 months after the start of treatment (visit 4). Visual analogue scale was used for evaluating pain and burning sensation and Thongprasom index for clinical improvement and healing. In addition, lesion sizes were measured and recorded at each visit using a grid.

RESULTS: Baseline characteristics, including pain and burning sensation score, size and clinical characteristics of the lesions according to Thongprasom index, were not different between the 2 treatment groups. Both AV and TA significantly reduced visual analogue scale score, Thongprasom score and size of the lesions after treatment ($P < 0.001$) and after 2 months of discontinuation of the treatment ($P < 0.001$). In the AV group, 74% of patients and in the TA group 78% of patients showed some degrees of healing in the last follow-up.

CONCLUSIONS: AV mouthwash is an effective substitute for TA in the treatment of OLP.

[Aloe vera oral administration accelerates acute radiation-delayed wound healing by stimulating transforming growth factor- \$\beta\$ and fibroblast growth factor production](#)

Am. J. Surg., Jun 2011; Vol. 201, No. 6, June 2011

Abstract

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

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

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

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

[In vitro study of the PLA2 inhibition and antioxidant activities of Aloe vera leaf skin extracts](#)

Abstract

BACKGROUND: In the present work we determined the total phenolic content of Aloe vera leaf skin (AVLS) extracts by using various solvents (hexane, chloroform-ethanol (1/1), ethyl acetate, butanol and water). We have also evaluated the antioxidant and the anti-PLA2 properties of these extracts by measuring their inhibition potency on the human pro-inflammatory phospholipase A2 (group IIA).

RESULTS: The water extract exhibits the highest inhibitory effect with an $IC_{50} = 0.22$ mg/ml and interestingly no effect was observed on the digestive phospholipase A2 (group IB) even at a concentration of 5 mg/ml. Antioxidant activities were also analyzed and the most active extracts were observed when using chloroform ethanol (1/1) and ethyl acetate ($IC_{50} = 0.274$ and 0.326 mg/ml, respectively). Analysis of the total phenolic content reveals that the water extract, with the best anti-PLA2 effect, was poor in phenolic molecules (2 mg GAE/g). This latter value has to be compared with the chloroform-ethanol and the ethyl acetate extracts (40 and 23.8 mg GAE/g, respectively), mostly responsible for the antioxidant activity.

CONCLUSION: A significant correlation was established between the total phenolic content and the antioxidant capacity but not with the anti PLA2 activity. Results from phytochemical screening suggest that the anti PLA2 molecules were probably catechin tannins compounds.



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REGULATORY NEWS

Latest Proposition 65 Settlement Proposed for \$80,000; Complaints Continue to Be Filed

by Michael McGuffin, AHPA President

Starting in April 2010 and as of June 14, 2011, a private plaintiff, San Diego, Calif.-based Environmental Research Center (ERC), has issued 223 (1) Proposition 65 notices—including almost 100 in 2011 alone—against 136 separate companies. Each of these notices alleges exposure to lead (and in one case to arsenic) by one or more dietary supplements or other natural products. Under California's Proposition

65, "The Safe Drinking Water and Toxic Enforcement Act of 1986," a product that exposes a consumer to more than 0.5 mcg per day of lead is generally required (1) to bear a "clear and reasonable" warning that the product contains lead and that lead is "known to the State of California to cause birth defects or other reproductive harm."

Only nine of the companies who have received notices from ERC have subsequently been named in complaints, which is the next step in the legal process through which a notice is resolved. One such complaint was filed in September 2010 against 1338299 Ontario, doing business as Integrity Marketing, in the matter of its product, Internal Flush®. Five retail chains were identified in separate notices as resellers of this product (2), which ERC alleged to "cause exposures to lead and lead compounds."

Proposition 65: The Options

Companies that sell dietary supplements and other natural products, such as protein powders and green foods, need to be aware of their options in dealing with Proposition 65, especially as the law affects the presence of lead in these products. These include:

- **Stay Out:** Restrict your sales to exclude all California commerce, including Internet sales and sales made by 3rd-party distributors
- **Stay Small:** Limit the number of your employees to not more than nine
- **Analyze for Lead Speciation:** Confirm that any lead present at over 0.5 mcg/day at the highest-labeled daily dose is "naturally occurring" and so is present "solely as a result of natural geologic processes."

Consultations with numerous AHPA members indicate that the three points above are not realistic options for most companies. The California marketplace is essential to most natural product sales; only the smallest firms can comply with the small company exemption; the burden of proving that lead is naturally occurring rests squarely on marketers and is a costly

process, especially for companies with numerous ingredients. That leaves the following options:

- **Analyze and Limit:** Do not be the second one to know how much lead is in your product! AHPA has reached agreements with analytical labs that provide significant discounts to AHPA members, and they will let you know if your products contain more than 0.5 mcg/day of lead. Contact [Steven Dentali](#) for more information.
- **Warn:** Provide the required clear and reasonable warning on any product lot with greater than 0.5 mcg/day of lead. Several companies have now taken this approach, and it may come to be that this labeling will become more common, so that most products in some classes will all provide the same information to consumers. Contact [Michael McGuffin](#) if you want to discuss this option further.
- **Wait to Get Sued:** The average settlement to date in the natural products category is just over \$150,000, which does not include legal expenses. Wouldn't you rather make a donation to the [AHPA-ERB](#)

[Foundation](#) instead? The only feasible ways to avoid this last option, in the face of the ongoing attention to the supplement product class, are either to analyze your products and keep them below 0.5 mcg/day of lead, or consider the use of product-warning labels.

Are there other options? Many in the industry have suggested that new ideas need to be explored. It is generally agreed though that the likelihood of having the Proposition 65 law overturned is very low; the state legislature can only amend it by a two-thirds majority and only "to further its purposes," and there is little evidence to suggest that the citizenry would vote to overturn the "Safe Drinking Water and Toxic Enforcement Act" (Proposition 65's formal name). The idea of federal preemption has been examined for many years with no success.

If you have any new ideas on this issue, please contact [Michael McGuffin](#) to discuss them. But in the meantime, the first five of the above options must be considered by all marketers doing business in California—as the last one is the default option and will be selected not by you, but by a private plaintiff.

A proposed, stipulated-consent judgment, signed by both ERC and Integrity Marketing on April 18, 2011, has now been filed in the California Superior Court in Marin County. The judgment would result in total settlement costs of \$80,000, presumably to be borne by Integrity Marketing rather than by the retailer defendants, each of whom is released from all claims under the terms of the proposed judgment.

American Herbal Products Association (AHPA) members have been informed on numerous occasions over the past year of the activities of ERC in targeting supplement products. The activities of this plaintiff were first reported last summer to call attention to ERC's first 52 notices, all of which had been issued in the prior four months (1). Subsequent articles noted this plaintiff's continued attention to the supplement class (3, 4) and recorded a developing focus by ERC on green foods and products in the sports supplement category (5).

In addition, AHPA and its Proposition 65 counsel, Trent Norris, from the firm Arnold & Porter, have prepared a document that is essential to understanding the impact of this law for supplement companies. Any AHPA member can obtain the document, *Background on California Proposition 65: Issues related to heavy metals and herbal products*, by [downloading](#) it. A more complete review of the issue is available in the form of AHPA's educational symposium, *Living with Proposition 65: Preventative Measures & Defending Against a 60-Day Notice*, which can be purchased at the [AHPA Bookstore](#).

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FDA Enforcement: FDA is Fighting Crime, and Warning Letters Should be Heeded

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

Modern Food and Drug Agency (FDA) criminal enforcement is often implemented following the old-fashioned procedure of following up on complaints and then investigating them. In this case, a complaint that a woman suffered adverse events after a treatment led to an investigation. The result? A San Francisco man was arrested and charged with introducing misbranded drugs into interstate commerce. The defendant is alleged to have sold Liu Shen Wan, also known as "Six God Tablets" or "Six Spirit Pills," as a traditional Chinese remedy for colds, flu, and other ailments from his business, Feng's Holistic Healing Center, also known as China House Clinic. The pills were found to contain arsenic and bufotenine, a Schedule I controlled substance found in toad venom. The FDA press release on this criminal investigation is [here](#).

And what happens to those companies that are found to be trafficking in drug-spiked supplements? Tribavus/IForce distributed the products "17aPheraFLEX," "Dymethazine" and "Methadrol" as dietary supplements. FDA found that these products contained synthetic steroids, known as DMT or Madol and Superdrol. Thus, these products were not dietary supplements but rather unapproved drugs under the Food, Drug, and Cosmetic Act. Tribavus Enterprises agreed to pay a \$125,000 fine and implement a testing protocol for its products to ensure future products sold as dietary supplements do not contain synthetic steroids. The FDA press release on this criminal investigation is [here](#).

And *never* use FDA Warning Letters as the basis for stocking and selling a product. Three men were indicted

for that with respect to selling the drug-spiked products “MASS XTREME” and “TREN XTREME”. The FDA press release on this criminal investigation is [here](#).

Thinking of ignoring a Warning Letter? Think again. Remember *severe acute respiratory syndrome* (SARS) and all the “treatments” that appeared? That near-pandemic situation between November 2002 and July 2003 resulted in 8,422 known infected cases and 916 confirmed human deaths worldwide. In 2005, FDA sent a Warning Letter to Sami Arshak Yanikian, informing him that he was marketing a drug and that he was making claims about his products, including ones regarding SARS, even though there was no evidence that they were generally recognized as safe and effective for their labeled uses. Yanikian responded to FDA, saying that he was selling the products abroad. However, as the jury heard during the subsequent trial, Yanikian actually sold his products to an undercover agent in Tempe, Ariz. Verdict: guilty. The FDA press release announcing Yanikian’s conviction can be found [here](#).

You would think that the many Warning Letters to those marketing colloidal silver products would be signals to those who market these products not to make disease claims. Nope. Natural Path/Silver Wings learned that such claims cause their products to be unapproved new drugs in a [Warning Letter](#). And FDA’s inspection of the facility uncovered numerous dietary supplement cGMP infractions. Interestingly, the company was first inspected, and then FDA looked at its website and found the drug claims. The lesson here is that when FDA inspects your facility, address all the problems—even the ones FDA did not note during its inspection. Often, companies correct what is noted in an FDA 483 Notice of Observations after an inspection or in a Warning Letter, and then fail to correct other issues and claims.

FDA expects all matters to be addressed. That’s just old-fashioned law enforcement.

* * *

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USDA Releases Final Guidance for Organic Wild-Crop-Harvesting Program

The United States Department of Agriculture (USDA) released the final version of its [guidance](#) for wild-crop harvesting under the National Organic Program on May 6, 2011, with an effective date of May 9, 2011. The guidance provides clarification on ways that accredited certifying agents and certified operations can demonstrate compliance with the wild-crop-harvesting [regulations](#) in 7 CFR 205.207.

American Herbal Products Association (AHPA) submitted comments on a [draft version](#) of this guidance in December 2010 and noted several sections in the draft guidance where its unclear language could have led to an adverse impact on current harvesting and manufacturing activities utilizing organic wild crops.

The final guidance clearly took AHPA comments into account, clarifying that minimal agricultural practices necessary for sustainable harvesting are specifically allowed (and occasionally required by local laws) in wild-crop harvesting. It provides examples of this. The revised guidance also notes explicitly that the presence of other rare, threatened, or endangered species in an area does not prevent wild-crop-harvesting operations to take place if possible and/or actual impacts of harvesting activities are described and addressed. Similarly, AHPA suggested that inspection criteria explicitly allow inspectors to interview a sample of crop harvesters as opposed to each and every one, and this was also implemented in the final version of the guidance.

“It is always pleasing to see federal agencies effectively working with and involving industry in guidance development,” said AHPA President Michael McGuffin upon reviewing the final version of the guidance. “It still remains to be seen how well the completed guidance meets its intended objectives with actual harvesting operations.”

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