Regulatory Compliance – Focus on US Issues

Len Monheit, Executive Director, Engredea
The premiere digital marketplace that connects the healthy lifestyle industry

We bring you the information on healthy living - from recipes to supplements to sustainability. We connect you to your next customer, and provide you with the sourcing, market research, standards and legislative information you need to grow your business.
Presentation Outline

• General themes
• International developments
• US regulatory update
• Future developments
General themes

• Safety first
• Watch claims and handling of new ingredients
• Export of regulation – lots of international dialogue
• Good Manufacturing Practices
International developments

• EU claims rejections
• Botanicals treated separately
• Adulterated products found
• Health claims crackdown
• International GMP
Introducing IADSA

• International Alliance Of dietary Supplement Associations (55 of which HADSA is one)

• Role:
  – Communication of regulatory, scientific and technical information about food supplements across the world.
  – Development of scientific and technical guidance to support regulation.
  – Advice to governments on regulatory models for dietary supplements.
IADSA's global GMP guide meets with strong demand

IADSA, NPI Center
Aug. 5, 2011 12:01am

Demand has soared across the globe for IADSA’s global Good Manufacturing Practices (GMP) guide with more than 600 copies downloaded from the IADSA website since its release in June.
Global Guide to Good Manufacturing Practice for Supplements

June 2011

The ‘Global Guide to Good Manufacturing Practice for Supplements’ gives guidelines for the promotion of best practice in the production of supplements, including manufacturing, quality control, packaging, distribution and storage. An important tool for both companies and governments worldwide, the guide covers quality management, premises and equipment, personnel and training, product and process development, manufacture, storage, transport and distribution. It also gives recommendations in areas critical to the manufacture of high quality products, including the recovery or re-working of materials, documentation, self-inspections, sub-contracting operations, laboratory testing, complaints procedures, product recall and emergency procedures.

Download
5 years to comply with EU nutrition labeling rules, says EAS

EAS, Engredea News & Analysis
Nov. 22, 2011 12:35pm

Food companies have five years to implement the mandatory nutrition labeling rules of the European Union’s Food Information to Consumers Regulation published today, said international policy experts EAS.

Xavier Lavigne, Food Law Manager at EAS, said that the clock starts ticking towards the five-year deadline for nutrition labelling requirements 20 days after publication, therefore from 13 December 2011.

The regulation requires a mandatory declaration on the label of the so-called ‘Big 7’ – energy, fat, saturated fat, carbohydrates, sugars, protein and salt – by 13 December 2016. It also requires these to be expressed per 100g/100ml and, where appropriate, per portion.

While most aspects of the regulation become applicable on 13 December 2014, companies have been given an extended transition period until 13 December 2016 to get in line with nutrition labelling requirements.

“The new food labelling regulation means inevitable changes for companies,” said Mr Lavigne. “The costs of conforming to the mandatory nutrient content rules will most likely hit the smaller food companies more than the larger ones, as many of the larger companies already have.
EU health claims: unanswered questions

Industry still in dark over nutrient profiling, botanicals, enforcement

Richard Clarke, Functional Ingredients
Dec. 2, 2011 3:05pm

In the fall, the European Commission published its draft list of permitted health claims, marking a significant step towards implementation—at last—of the EU’s Nutrition & Health Claims Regulation. But there are some unanswered questions.

In the fall, the European Commission published its draft list of permitted health claims, marking a significant step towards implementation—at last—of the EU’s Nutrition & Health Claims Regulation.

Once the list has been adopted into law, expected to be in the spring, the industry will have a transition period of six months to withdraw any claims not contained within it. It’s no exaggeration to say this will represent a revolution in the European market for functional ingredients.

But there are some unanswered questions.

For example, what has happened to the promised ‘nutrient profiling’ system? What does the future hold for botanical ingredients? And how will the law be enforced in national member...
Botanicals developments

• The European Botanical Forum (EBF) recently met with two representatives of the European Commission’s DG SANCO to discuss botanicals.

• The EBF’s position in the discussion can be summarised as follows:
  – Current legislation already covers the safety of botanicals.
  – A negative list (based on the negative list already prepared by the EBF) under Regulation 1925/2006 on the Addition of Nutrients to Foods, which has an annexe for substances with safety concerns, may be a good first step.
  – The development of further lists could be envisaged based on priority issues relating to safety. This should not be a closed positive list, but an open list.
  – Identification of physiological effects should be based on the principles of ECJ case law and homeostasis. EFSA opinions could be a useful source of information in this respect.
  – Indications/claims should be based on traditional use.
GLOBAL REGULATORY DEVELOPMENT
## New legislation in development

<table>
<thead>
<tr>
<th>Austria</th>
<th>Hungary</th>
<th>Norway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>India</td>
<td>Philippines</td>
</tr>
<tr>
<td>Brazil</td>
<td>Indonesia</td>
<td>Poland</td>
</tr>
<tr>
<td>Brunei</td>
<td>Ireland</td>
<td>Romania</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>Israel</td>
<td>Russia</td>
</tr>
<tr>
<td>Cambodia</td>
<td>Italy</td>
<td>Singapore</td>
</tr>
<tr>
<td>China</td>
<td>Japan</td>
<td>Slovakia</td>
</tr>
<tr>
<td>Colombia</td>
<td>Laos</td>
<td>South Africa</td>
</tr>
<tr>
<td>Croatia</td>
<td>Latvia</td>
<td>Spain</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Lithuania</td>
<td>Sweden</td>
</tr>
<tr>
<td>Cyprus</td>
<td>Luxembourg</td>
<td>Thailand</td>
</tr>
<tr>
<td>Denmark</td>
<td>Malaysia</td>
<td>Turkey</td>
</tr>
<tr>
<td>Estonia</td>
<td>Malta</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Finland</td>
<td>Mexico</td>
<td>Uruguay</td>
</tr>
<tr>
<td>France</td>
<td>Myanmar</td>
<td>Venezuela</td>
</tr>
<tr>
<td>Germany</td>
<td>Netherlands</td>
<td>Vietnam</td>
</tr>
<tr>
<td>Greece</td>
<td>New Zealand</td>
<td></td>
</tr>
</tbody>
</table>

**ASEAN & EU Harmonization**
Examples

EUROPE:
- New Food Law
- Maximum levels, Botanicals & Claims

RUSSIA:
- New Food Law

CHINA:
- New Health Food Provision

LATIN AMERICA:
- Category, Vit/Min Limits, Safety, Botanicals, Claims, Distribution

JAPAN:
- Health Claims

ASEAN:
- Health Supplement Harmonization
Clear Category

Dietary Supplements predominantly a sub-category under Food Law
Supplement Terminology

- **Codex:** Vitamin & Mineral Food Supplements
- **USA:** Dietary Supplements
- **Europe:** Food Supplements
- **Japan:** Foods (no supplement category)
- **Korea:** Health Functional Foods
- **China:** Health Foods
- **ASEAN:** Health Supplements
- **Russia:** Biologically Active Supplements
- **Canada:** Natural Health Products
- **Australia:** Complimentary Healthcare Products
Definition

**Purpose**
To supplement the diet

**Role**
To provide nutrients or other substances with a nutritional or physiological effect

**Content**
Include a range of substances, whether natural or synthetic, ranging from vitamins and minerals to plants and substances of animal and mineral origin

**Form**
Capsules, tablets, liquids, powders etc
Ingredients

- Vitamins and minerals
- Botanicals and botanical extracts
- Other substances, such as:
  - Amino acids and derivatives
  - Enzymes
  - Pre- and Probiotics
  - Essential Fatty Acids
# Category, Definition & Ingredient Trends

<table>
<thead>
<tr>
<th>Category Name</th>
<th>ASEAN In process</th>
<th>China Health Food</th>
<th>EU Food Supplement</th>
<th>Japan Food</th>
<th>Korea Health Functional Food</th>
<th>Russia Biological Active Substance</th>
<th>USA Dietary Supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categorization</td>
<td>? to be defined</td>
<td>Food</td>
<td>Food</td>
<td>Food</td>
<td>Food</td>
<td>Food</td>
<td>Food</td>
</tr>
<tr>
<td>Vitamin &amp; Minerals</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Botanicals</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Other Substances</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(i.e. fish oil, probiotics)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Variability in number of ingredients & system of authorization
# Allowance of Ingredients

<table>
<thead>
<tr>
<th>Market</th>
<th>Allowed “Existing” Ingredients</th>
<th>“New” Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU</td>
<td>• Used before 1997 (FS Directive)</td>
<td>• Novel Ingredient authorization</td>
</tr>
<tr>
<td></td>
<td>• Vitamin &amp; Mineral positive list</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Other Ingredients regulated at Member States level – some Positive</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>• Used before 1994 (DSHEA)</td>
<td>• New Dietary Ingredient (NDI) notification</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(exempt from notification if in food supply)</td>
</tr>
<tr>
<td>ASEAN</td>
<td>• Negative list</td>
<td>• Self assessment of safety and not meet criteria for inclusion in Negative list</td>
</tr>
<tr>
<td></td>
<td>• Restricted condition of use list</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>• Positive list for use in foods</td>
<td>• Self or Government assessment if food or drug ingredient</td>
</tr>
<tr>
<td></td>
<td>• List of not drug ingredient</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Part of food supply</td>
<td></td>
</tr>
<tr>
<td>Korea</td>
<td>• Health Functional Food (HFF) Code</td>
<td>• New HFF Ingredient authorization</td>
</tr>
<tr>
<td></td>
<td>• Part of food supply</td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>• Positive list for use in foods &amp; drugs</td>
<td>• no specified regulation/process</td>
</tr>
<tr>
<td></td>
<td>• Positive list for use in health foods</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Negative list for use in health foods</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Part of food supply</td>
<td></td>
</tr>
</tbody>
</table>
Vitamin & Mineral Maximum Levels

- RDA was a traditional approach → **Focused on nutrient sufficiency**
- Growing understanding that optimum intakes may be higher than RDA; RDA better for developing minimum requirements
- Recognition that as long as safe, there should be the possibility for consumers to have a choice of products → **Scientific Risk Assessment**
- Reflected in the last decade in key international laws and standards
  - EU 2002
  - Codex 2005
  - China 2005
  - Korea 2008
  - ASEAN 2009
- Other markets using safety basis: US, Russia, Canada, Australia
Market Approach to Maximum Levels

Safety Based
- EU (27 markets)
- ASEAN (10 markets)
- USA
- Korea
- Japan
- Russia
- Australia
- Canada
- Argentina
- Colombia
- Costa Rica

RDA based
- Brazil
- Chile (discussion underway on safety-based limits)
- Mexico
- Cambodia*
- Laos*
- Philippines*
- Thailand*

* Market moving to safety based levels within ASEAN Harmonization
US developments

• Food Safety Modernization Act
  – New enforcement powers to FDA
  – Dietary ingredients affected (HACCP approach)

• Foods and supplements intersection (Lazy cakes)

• Beverages and supplements intersection

• DSHEA
  – Claims
  – GMPs
  – New Dietary Ingredients (NDI)
FDA on global trade (June 2011)...

• "Global production of FDA-regulated goods has exploded over the past ten years. In addition to an increase in imported finished products, manufacturers increasingly use imported materials and ingredients in their U.S. production facilities, making the distinction between domestic and imported products obsolete," said Commissioner of Food and Drugs Margaret A. Hamburg, M.D. "There has been a perfect storm - more products, more manufacturers, more countries and more access. A dramatic change in strategy must be implemented."
FDA issues first new rules under Food Safety Modernization Act

The U.S. Food and Drug Administration announced two new regulations that will help ensure the safety and security of foods in the United States. The rules are the first to be issued by the FDA under the new authorities granted the agency by the FDA Food Safety Modernization Act (FSMA), signed into law by President Obama in January. Both rules will take effect July 3, 2011.

The first rule strengthens FDA's ability to prevent potentially unsafe food from entering commerce. It allows the FDA to administratively detain food the agency believes has been produced under insanitary or unsafe conditions. Previously, the FDA's ability to detain food products applied only when the agency had credible evidence that a food product presented was contaminated or mislabeled in a way that presented a threat of serious adverse health consequences or death to humans or animals.

Beginning July, the FDA will be able to detain food products that it has reason to believe are adulterated or misbranded for up to 30 days, if needed, to ensure they are kept out of the marketplace. The products will be kept out of the marketplace while the agency determines whether an enforcement action such as seizure or federal injunction against distribution of the product in commerce, is necessary.

Before this new rule, the FDA would often work with state agencies to embargo a food product under the state's legal authority until federal enforcement action could be initiated in federal court. In keeping with other provisions in the FSMA, FDA will continue to work with state agencies on food safety and build stronger ties with those agencies.

“This authority strengthens significantly the FDA's ability to keep potentially harmful food from reaching U.S. consumers,” said FDA Deputy Commissioner for Foods Mike Taylor. “It is a
FDA NEWS RELEASE

For Immediate Release: October 11, 2011
Media Inquiries: Pat El-Hinnawy, 301-796-4763, Patricia.El-Hinnawy@fda.hhs.gov
Consumer Inquiries: 1-888-INFO-FDA

FDA: U.S. Marshals seize foods stored at Washington State facility
FDA inspection found rodent and insect infestation

At the request of the U.S. Food and Drug Administration, U.S. Marshals seized food products held at the food storage and processing facility of Dominguez Foods of Washington, Inc., in Zillah, Wash., on Sept. 30, 2011.

The seized products had been subject to a detention order issued by FDA on Sept. 2, 2011, following an FDA inspection of the facility that found evidence of widespread and active rodent and insect infestation in the facility’s warehouse and processing area.

In a complaint filed Sept. 29, 2011, the United States alleged that the detained food was adulterated under the Federal Food, Drug, and Cosmetic Act (FFDCA) due to the conditions in the warehouse documented during FDA’s inspection. The complaint asked the Court to issue a warrant of arrest for the products, which directed the U.S. Marshals to seize the products, and requested that the Court condemn and forfeit the food to the United States. The U.S. District Court for the Eastern District of Washington issued a warrant of arrest for the products the same day.

The action represents the first seizure of food subject to an FDA detention order. Pursuant to the FFDCA, as amended by the FDA Food Safety and Modernization Act, FDA may order the detention of food found during an inspection when the investigator has reason to believe that such food is adulterated or misbranded. Food subject to an FDA detention order may not be transferred from the place at which it is detained until it is released by FDA or the detention order expires. A detention order may remain in place for up to 30 days to allow FDA to take appropriate action under the FFDCA, such as seizure.

"FDA will not hesitate to take immediate steps to protect the public’s health," said Dara A. Corrigan, the FDA’s associate commissioner for regulatory affairs. “We will aggressively use our enforcement tools to prevent adulterated food from reaching the public.”

During their inspection of the Dominguez Foods facility, FDA investigators observed rodent droppings and urine stains on and around food products, rodent gnawed containers of food, a rodent nesting site, and one dead rodent in the warehouse, as well as live and dead insects in, on, and around food products. The investigators took immediate action, issuing a detention order covering all of the food in the facility not in hermetically sealed containers at the end of their inspection.
FOOD AND DRUG ADMINISTRATION

Better Coordination Could Enhance Efforts to Address Economic Adulteration and Protect the Public Health

Why GAO Did This Study

In recent years, the United States experienced public health crises suspected to have been caused by the deliberate substitution or addition of harmful ingredients in food and drugs—specifically melamine in pet food and oversulfated chondroitin sulfate in the blood thinner heparin. These ingredients were evidently added to increase the apparent value of these products or reduce their production costs, an activity GAO refers to as economic adulteration. The Food and Drug Administration (FDA), an agency within the Department of Health and Human Services (HHS), has responsibility for protecting public health by ensuring the safety of a wide range of products that are vulnerable to economic adulteration. This report examines (1) the approaches that FDA uses to detect and prevent economic adulteration of food and medical products and (2) the challenges FDA faces in detecting and preventing economic adulteration and views of stakeholders on options for FDA to enhance its efforts to address economic adulteration. GAO reviewed FDA documents and interviewed FDA officials and stakeholders from academia and industry, among others.

What GAO Found

FDA primarily approaches economic adulteration as part of its broader efforts to combat adulteration in general, such as efforts to ensure the safety of imported products. Agency officials noted that the Federal Food, Drug, and Cosmetic Act does not distinguish among motives or require motive to be established to determine whether a product is adulterated. However, a senior FDA official told GAO that there is value in making a distinction between economic adulteration and other forms of adulteration to guide the agency’s thinking about how to be more proactive in addressing this issue. An FDA official told GAO when the agency detects any form of adulteration that poses an adverse public health effect, it can conduct an investigation, request a recall to get the product off the market, and take enforcement action. In addition to these broader efforts, some FDA entities also have undertaken efforts that specifically focus on economic adulteration. For example, FDA’s Office of Regulatory Affairs has contracted with a research center to model risk factors for improved detection of economic adulteration of food. However, FDA entities have not always communicated or coordinated their economic adulteration efforts. For example, FDA’s Center for Veterinary Medicine was unaware of and did not participate in two other entities’ economic adulteration efforts involving products the veterinary center regulates. In another instance, two FDA entities engaged in similar efforts but did not communicate or coordinate them, even though officials said such communication might be beneficial. Furthermore, FDA has not issued specific written guidance on how its centers and offices should approach or address their economic adulteration efforts. This is not consistent with federal standards for internal control, which require agencies to have documented policies and procedures.

FDA officials and stakeholders GAO interviewed cited several key challenges to detecting and preventing economic adulteration, including increased globalization and lack of information from industry. Globalization has led to an increase in the variety, complexity, and volume of imported food and drugs, which complicates FDA’s task of ensuring their safety. In addition to globalization, an increase in supply chain complexity—the growth in the networks of handlers, suppliers, and middlemen—also complicates FDA’s task, making it difficult to trace an ingredient back to its source. FDA officials and stakeholders also said that gathering information from industry, such as information on potentially adulterated ingredients, presents challenges for FDA in detecting and preventing economic adulteration due to industry’s reluctance to share such information because it is proprietary. Stakeholders cited greater oversight and information sharing as options to improve FDA’s ability to combat economic adulteration. Specifically, some stakeholders supported increased oversight, such as the use of technology to trace adulterated ingredients back to the point of contamination, as an option to obtain more information on supply chains. Many stakeholders also suggested that FDA increase its regulatory and enforcement actions to address economic adulteration, including in instances that may not have a large negative public health impact. Stakeholders also suggested that greater communication with industry, through means such as an information clearinghouse or more informal interactions, could enhance FDA efforts to gather information on economic adulteration.

What GAO Recommends

GAO recommends that FDA adopt a working definition of economic adulteration, enhance communication and coordination of agency efforts, and provide guidance to agency centers and offices on the means of addressing economic adulteration. HHS neither agreed nor disagreed with GAO’s recommendations, but cited planned actions related to adopting a definition and enhancing communication and coordination.

United States Government Accountability Office
On GMPs

- FDA Warning Letters to dietary supplement manufacturers are becoming more detailed, now frequently citing the failure to have specifications for purity, strength, and composition of finished supplement batches, with one letter noting that no response had been submitted to the FDA on 483 issues noted by the FDA inspector.
Consistent Breaches

• Patterns are emerging from recent inspections.
• Manufacturing records, ingredient identity, training records, supplier qualification, quarantine are areas of specific focus .... And identified problems
• And the audits are expected to get more intense
Consistent Breaches
FDA NEWS RELEASE

For Immediate Release: Nov. 23, 2011

Media Inquiries: Pat El-Hinnawy, 301-796-4763 or 202-557-6531, patricia.el-hinnawy@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA takes enforcement action against Pennsylvania dietary supplement maker

First permanent injunction of its kind; more than 400 products affected

The FDA today took legal action against a dietary supplement maker and owner for substituting ingredients and products without noting the changes on the final product labels. The permanent injunction, filed on behalf of the FDA by the U.S. Department of Justice, would stop the defendants from making and distributing more than 400 products for being in violation of the Federal Food, Drug, and Cosmetic Act.

This is the first time FDA has taken legal action against a dietary supplement manufacturer of this size for failure to comply with the dietary supplement current Good Manufacturing Practice (cGMP) regulations. The cGMPs for dietary supplements went into effect in 2007, in a stepped process based on company size. This company’s compliance date came into effect in 2010, and they did not meet the relevant cGMP requirements after that date.

The FDA requested the permanent injunction against ATF Fitness Products Inc. (ATF), Manufacturing ATF Dedicated Excellence, Inc. (MADE), and James G. Vercellotti of Oakmont, Pa., owner and operator of both companies. The cGMP regulations require manufacturers to ensure quality in their dietary supplements by controlling all aspects of their processes and procedures. MADE makes more than 400 dietary supplements, including vitamins and minerals, under the brands “Sci-Fit,” “Nature’s Science” and “For Store Only.” ATF purchases dietary supplements exclusively from MADE and distributes them throughout the United States.
On May 25 - June 24, 2011, the U.S. Food and Drug Administration (FDA) conducted an inspection of your facility, located at 12245 SW 128th St. Unit 301, Miami, Florida. The inspection revealed serious violations of FDA’s Current Good Manufacturing Practice (CGMP) in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements, Title 21, Code of Federal Regulations, Part 111 (21 CFR Part 111). At the conclusion of the inspection, you were issued a Form FDA 483, List of Inspectional Observations, which listed a number of the violations that cause your dietary supplement products, Milk Thistle and L-Carnitine, to be adulterated within the meaning of section 402(g)(1) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 342(g)(1)] in that the products have been prepared, packed, or held under conditions that do not meet CGMP requirements for dietary supplements.

In addition, FDA collected and reviewed samples of the labeling of your dietary supplement and cosmetic products during the inspection of your facility. Based on our review of your product labels, we have determined that your products, Nutra Stress Tablets, Tri-flex Capsules, Noni Juice, Arthritis Formula Capsules, and Prostagard Capsules, are promoted for conditions that cause them to be drugs within the meaning of section 201(g)(1)(B) of the Act [21 U.S.C. § 321(g)(1)(B)]. The therapeutic claims on your labels establish that the products are drugs because they are intended for use in the cure, mitigation, treatment, or prevention of disease.

Furthermore, your products, Cardispan Levo carnitina and Collagen Cream With Dribble of the Snail, are cosmetics within the meaning of section 201(i) of the Act [21 U.S.C. 321(i)] because they are intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance. As such, FDA has determined that these cosmetic products are misbranded within the meaning of section 602(a) of the Act [21 U.S.C. § 362(a)] because the ingredients in each product are not listed on the label in accordance with 21 CFR 701.3.

You can find the Act and its implementing regulations through links on FDA’s home page at http://www.fda.gov.

The significant violations are the following:

**Adulterated Dietary Supplements**

1. You failed to verify that a subset of your finished batches of dietary supplements that you identify through a sound statistical sampling plan, or every finished batch, meet finished product specifications for identity, purity, strength, composition, as required by 21 CFR 111.75(c).

Specifically, during the inspection you stated that you do not perform any finished product testing to verify the identity, purity, strength and composition of your dietary supplement products. Furthermore, your batch records for the following released finished products lacked finished product testing to verify the identity, purity, strength, and composition:

- Milk Thistle batches 3827 dated 9/20/10, 3827 dated 9/23/10, 3652 dated 7/13/10, and 4295 dated 6/3/11;

In your response letter dated July 12, 2011, you stated you have hired a second consultant to develop raw material specifications and that you will send raw materials to a contract laboratory for identity testing with a completion time of six months. We find this response inadequate in that you have not addressed finished product testing or the development of specifications of finished products, as required by 21 CFR 111.70(e).

2. You failed to confirm the identity of other components (not including dietary ingredients) and determine whether other applicable component specifications established in accordance with 21 CFR
Department of Justice Office of Public Affairs FOR IMMEDIATE RELEASE Wednesday, November 30, 2011 Two New Jersey Dietary Supplement Firms and Their Principals Sentenced for Criminal Contempt
WASHINGTON – New Jersey-based dietary supplement companies Quality Formulation Laboratories Inc. (QFL) and American Sports Nutrition Inc. (ASN), as well as their owner, Mohamed S. Desoky, and managers, Ahmad Desoky Esq., and Omar Desoky, were sentenced today for multiple counts of criminal contempt of court for violating a consent decree entered by the U.S. District Court for the District of New Jersey on March 16, 2010, the Justice Department announced.

The defendants’ businesses manufactured and distributed food products and supplements, including many varieties of protein powder mixes sold in health food stores, as well as other powder mixes and dietary supplements. The defendants’ products were distributed under the ASN brand to locations throughout the United States.

U.S. District Court Chief Judge Garrett E. Brown Jr. sentenced Mohamed S. Desoky to a term of 40 months in prison, three years supervised release and a fine of $60,000; Ahmad Desoky Esq., to a term of 34 months in prison, three years supervised release and a fine of $12,000; and Omar Desoky to a term of 34 months in prison and three years supervised release. In addition, Judge Brown ordered QFL and ASN to pay criminal fines totaling $1 million, and placed them on probation for a period of three years. All defendants, the individuals and the corporations, were prohibited from doing business in the dietary supplement industry during their periods of supervised release or probation unless they first obtained consent of the U.S. Food and Drug Administration and the Court. Ahmad Desoky was barred from practicing law during his period of supervised release. In imposing sentence, the court commented that defendants’
On NDIs

• Most important FDA document in years even though it’s a draft guidance
• FDA’s position is that an NDI is required for every unique combination of ingredients (ie. On the finished product)
• Other key issues:
  – what makes it a NEW ingredient...new technology, new solvents, new process?
  – How do you prove an old ingredient
  – NDI versus GRAS (Generally Recognized as Safe)
  – Synthetic equivalents of natural ingredients
NDI’s – a requirement under the law since 1994

- Was in DSHEA – one page at least although inadequately considered
- Law never specified how to comply – only said submit
- Extraction technologies like super-critical fluid extraction – did not exist commercially in 1994
- “Takes ingredients to food additive status, undoing hard-won gains”
- Will have industry arguing, debating and taking legal action for years
- Effect on innovation and IP?
NDI’s – the real issues

- An Ingredient or a Finished Dietary Supplement Product
- Who Must File a New Dietary Ingredient Notification?
- Old Dietary Ingredient Authoritative Lists (associations and HOC)
- Synthetic Botanicals Are Not Dietary Ingredients...?
- Microbial Dietary Ingredients – Are They Biologics in FDA’s View?
- Food Additive Safety Requirements for Dietary Supplements are Inconsistent with DSHEA
- Chemical Alteration – a prescriptive list of processes allowed or principle based approach?
- Protection of NDI Submitter’s Intellectual Property
General NDI Decisions

• Is it a dietary ingredient?
• Is it new?
• Is it subject to notification?
• What information should be submitted?
Is it a dietary ingredient per DSHEA

- 21 U.S.C. 321 (ff)(1)
  - (A) a vitamin
  - (B) a mineral
  - (C) an herb or other botanical
  - (D) an amino acid
  - (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
  - (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)
Examples of herbal dietary ingredients

- An herb: chamomile flower; ginkgo leaf; saw palmetto fruit
- An other botanical: tomato fruit
- A concentrate of an herb / botanical: tomato paste
- A metabolite of an herb or other botanical: matricin
- A constituent of an herb or other botanical: ginkgo flavonoid glycosides; lycopene
- An extract of an herb or other botanical: chamomile aqueous-ethanolic tincture; saw palmetto CO₂ extract
- A combination of any above (w/ or w/out other DIs)
Is it a dietary ingredient?

- marketed in the U.S. <DSHEA
- introduced in U.S. >DSHEA
- (ff)(1)(F) herbal DI if:
  - A concentrate, metabolite, or combination
  - **A naturally occurring constituent, but NOT a synthetic constituent**
  - An extract, irrespective of solvent
- (ff)(1)(E) herbal DI “for use by man to supplement the diet…”
Is it a new dietary ingredient?

- (ff)(1)(C) herbal DI marketed in the U.S. <DSHEA
  - As a DS or DI (inc. in a blend) but NOT as a conventional food, drug, or non-food
  - FDA says no “authoritative list”
    - Herbs of Commerce-2 (2000) specific to <DSHEA use
New Dietary ingredient

• (ff)(1)(F) DI if:
  • A concentrate, metabolite, non-synthetic constituent, extract or combination that has not been chemically-altered from <DSHEA form, AND
  • … was marketed <DSHEA as a DS or DI but NOT as a conventional food, drug, or non-food

• (ff)(1)(E) DI “for use by man to supplement the diet…”

• But not….
  • An extract of an ODI with solvent other than water or aqueous ethanol
  • Any change to manufacturing process of an ODI or NDI that alters its chemical composition or structure
On NDI notifications

Is a notification required?

- ANY new DI (per prior slide) UNLESS:
  - The DI is an article used for food AND in a form that has not been chemically altered (≠ minor loss of volatile components, dehydration, lyophilization, milling, and formation of a tincture or a solution in water, a slurry, a powder, or a solid in suspension
  - The DI is listed or affirmed by FDA as GRAS, self-affirmed as GRAS, or approved as a direct food additive in the U.S.
Examples of chemical alteration

- Removal of some components of a tincture (e.g., by chromatography, distillation or membrane filtration), which changes the chemical composition of the mixture.
- Use of solvents other than water or aqueous ethanol since other solvents alter the composition of the extract by extracting different types of constituents.
- Application of nanotechnology.
- Changing agricultural conditions to alter the chemical composition of the ingredient.
- Use of a botanical ingredient that is at a different life stage than previously used.
What information to submit?

- To identify the herbal DI (if (ff)(1)(C)) or herbal source of the DI (if (ff)(1)(F)):
  - Latin name including author citation
  - Plant part
  - Voucher specimen
  - Conditions of propagation and cultivation, including seasons
  - Geographic origin
  - Controls for known toxins
What information to submit?

• To describe the production method
  • As necessary “to demonstrate that it is the same as or similar to the botanical materials described in information submitted as evidence of the safety of the NDI.”

• To describe an extract or concentrate:
  • Overview of the manufacturing process; should clarify identity of final product and relationship to starting material.
  • Description and amount of all added ingredients, including solvents / solvent residues.
  • Concentration or dilution ratio, or range of concentration or dilution ratios.
  • Quantitative content of “any marker substances.”
  • Methods to insure batch to batch consistency.
  • Controls for adulterants (non-food solvents, pesticides, heavy metals, filth).
What information to submit?

Safety information / History of safe use:

- Evidence of safe use as a food or DS (or as a component) at levels ≤ the NDI level; e.g:
  - Historical dose and daily intake, duration and frequency of use, additional information on historical conditions of use.
  - Published data and information, reports from authoritative bodies, survey data, cookbooks or other published recipes, proprietary survey or consumption data, product sales data, and compositional analyses.
What information to submit?

- **Safety information / History of safe use:**
  - Data on history of use in humans should be the first evidence considered in evaluating the safety of a NDI. When the NDI has been previously consumed by humans, additional animal or human safety data are seldom needed if (1) the proposed use level is similar to or less than the levels safely consumed by humans in the past, and (2) the population expected to consume the NDI is the same as, or a subset of, the population that safely consumed the substance in the past. In many cases, no additional animal or human safety data are needed.”
What information to submit?

- Safety information / Safety testing data:
  - Genetic toxicity tests.
  - A 14-day range-finding oral study to establish a maximum tolerated dose (MTD) in an appropriate animal model.
  - A 90-day sub-chronic oral study to establish MTD and NOAEL
  - A repeat-dose tolerability study in humans (30-90 days)
  - A one-year chronic toxicity study in an appropriate animal model or a two-year carcinogenesis study in rodents.
  - Multi-generation rodent reproductive and teratology study.
  - NOTE: Last not needed if not for use by pregnant or lactating women, women of childbearing age, and children under 14.
NDI Notifications to Date

- 547 Total notifications as of February, 2010
  - 64 Notifications for dietary supplements →
- 483 Total NDI notifications
  - 112 Resubmissions →
  - 361 Unique NDI notifications
    - 15 withdrawn or subject of an unclassifiable FDA response →
- 346 Unique / classifiable NDI notifications
NDI FDA Response Options

- “File” w/ or w/o substantive comments
- Object due to expressed “concerns”:
  - NOT expected to be safe
  - Not a dietary ingredient per DSHEA
  - Failure to conform with 21 CFR 190.6
  - Notification does not provide sufficient information to make a safety determination, usually because:
    - Insufficient ingredient characterization
    - Lack of direct relationship between submitted information and actual NDI
NDI Notifications >2001

- 384 Total NDI notifications
  - 47 “filed” on initial submission (15.4%)
  - 34 “filed” on resubmission (11.2%)
  - 224 w/ “concerns” so not filed (73.4%)
    - 79 resubmitted but still w/ “concerns”
NDI Notifications >2001

NDIs Only (no DS) 2001-2009

Annual Notifications
"Filed" by FDA
% "Filed"

<table>
<thead>
<tr>
<th>Year</th>
<th>Annual Notifications</th>
<th>Filed by FDA</th>
<th>Filed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>18</td>
<td>5</td>
<td>28%</td>
</tr>
<tr>
<td>2002</td>
<td>49</td>
<td>15</td>
<td>31%</td>
</tr>
<tr>
<td>2003</td>
<td>50</td>
<td>8</td>
<td>18%</td>
</tr>
<tr>
<td>2004</td>
<td>37</td>
<td>5</td>
<td>14%</td>
</tr>
<tr>
<td>2005</td>
<td>49</td>
<td>10</td>
<td>20%</td>
</tr>
<tr>
<td>2006</td>
<td>55</td>
<td>9</td>
<td>16%</td>
</tr>
<tr>
<td>2007</td>
<td>49</td>
<td>10</td>
<td>20%</td>
</tr>
<tr>
<td>2008</td>
<td>36</td>
<td>5</td>
<td>14%</td>
</tr>
<tr>
<td>2009</td>
<td>34</td>
<td>10</td>
<td>29%</td>
</tr>
</tbody>
</table>
FDA “concerns” since 2001 (384 submissions)

- The agency determines that the ingredient does not fit the definition of a dietary ingredient: \textbf{89}
  - Drug claims in submission
  - Forms: Chewing gum, lozenge or other sublingual
  - Various excluded IND drug ingredient ingredients: Cotinine; Porcine relaxin; trans-resveretrol; Benfotiamine; Sarcosine; \textit{Bacillus suptilis} Strain PB6; Hyaluronic acid
FDA “concerns” since 2001

- Failure to conform to 21 CFR 190.6: **80**
  - Common reasons given:
    - Failure to provide English translations of cited articles, or full articles for referenced abstracts
    - Daily serving level of NDI not stated
    - Latin name and author not given or incorrect
    - No “history of use or other evidence of safety”
    - Not submitted in triplicate
    - Not signed
    - [Only perfect provision: Name and address]
FDA “concerns” since 2001

- Insufficient information: 247
- “Unable to determine the identity” of the NDI
- Unclear how the NDI “is qualitatively or quantitatively similar to the material used in the studies” provided
- Questions as to whether the submitted information is actually a sufficient basis for supporting a reasonable expectation of safety
AHPA’s NDI Tools

- **AHPA NDI Database:** [http://ndi.npicenter.com](http://ndi.npicenter.com)
  - All NDI notifications; linked to all associated reports
  - Searchable by ingredient or company
  - Provides succinct “outcome statement”

- **Interim Guidance on NDI Notifications** (June 2011)
  - Legal & regulatory background
  - “How to” on filing an NDI notification; worksheets on:
    - Determination of requirement to submit
    - Submission of notification
    - Form for cover to submission

- **ODI (herbal/botanical) documentation records**
  - Web portal by end of 2011
  - In the meantime: mmcguffin@ahpa.org
Welcome to the AHPA NDI database.

Welcome
Welcome to the American Herbal Products Association (AHPA) New Dietary Ingredient (NDI) Database. This database compiles New Dietary Ingredient (NDI) notifications submitted to the Food and Drug Administration (FDA) for new NDIs that are used in dietary supplements.

About the AHPA NDI Database
AHPA’s staff regularly obtains NDI notifications upon their transmittal to FDA’s Division of Dockets Management (DDM) and maintains a database of more than 500 NDI notifications available in the AHPA NDI Database, which is the only up-to-date compilation of NDI notifications.

The AHPA NDI Database is a joint project of AHPA, which is responsible for its content, and NPlcenter, part of the Natural Products Industry Association, which provides technical support to maintain this site.
What’s Next?

• Comment period just ended
• Comment evaluation
• Legal options?
• Intercession?
• In the meantime – enforcement under the draft guidance
NPA calls for rewrite of NDI draft guidance

The Natural Products Association (NPA), Engredea News & Analysis  
Dec. 1, 2011 1:00pm

Leading representative of the dietary supplement industry submits formal comments to FDA.

The Natural Products Association (NPA) has submitted extensive comments to the Food and Drug Administration (FDA) in response to the agency’s draft guidance on New Dietary Ingredients (NDI).

“In this draft guidance, the FDA significantly oversteps the authority given to it by Congress in DSHEA,” said NPA Executive Director and CEO John Gay. “Therefore, a substantial rewrite of the guidance is necessary.”

“Congress set appropriate parameters regarding the safety of new dietary ingredients, and NPA supports those safety measures. Unfortunately, this draft guidance goes well beyond what was envisioned by Congress,” said NPA Vice President for Scientific and Regulatory Affairs Dr. Cara Welch. “To cite just one example, the draft guidance sets up a de facto food additive safety standard, which directly contravenes the intent of Congress in DSHEA.”

Added Gay, “Through DSHEA, Congress envisioned a system that would allow products already on the market to remain available to the consumer while creating a reasonable mechanism for new ingredients to enter the market. The draft guidance does neither. Rather, it proposes an NDI process that would result in dampened innovation, more expensive and fewer products, and excessive paperwork, robbing the industry and FDA of scarce resources. The overall impact would be felt by customers, retailers, and suppliers alike, hitting small businesses especially hard.”
CRN tells FDA it's time to start over on NDIs

Hank Schultz, Functional Ingredients
Dec. 2, 2011 11:57am

The Council for Responsible Nutrition has called upon the Food and Drug Administration to withdraw its draft guidance on New Dietary Ingredients, saying it “far exceeds the permissible scope of a guidance document, proposing substantive requirements that must be the subject of notice-and-comment rulemaking.”

What is in this article?:
- CRN tells FDA it’s time to start over on NDIs
- Improper use of food additive standards

More About: US Supplement Regulation

It is the second time in the past few days that a major industry group has asked FDA to start over on the NDI draft guidance. On Nov. 30, the Natural Products Association filed comments.
H.R. 3880, The Dietary Supplement Protection Act of 2011, filed by Congressman Dan Burton

SEC. 3. NEW DIETARY INGREDIENT DEFINITION.

Section 413(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350b(d)) is amended by striking “October 15, 1994” each place it appears and inserting “January 1, 2007”.
Future Developments

• More globalization
• Continued safety/risk-based assessment
• Limited enforcement resources so media used as the enforcement vehicle
• In the US:
  – More GMP problems
  – More focus on adulteration
  – More focus on residual solvents in ingredients
  – More arguing over what is an NDI
  – More burden on suppliers
PRESS RELEASE

EHPM voices concern over claims not in the Article 13.1 permitted list

5 December 2011

Article 13.1 health claims that have been given an unfavourable EFSA opinion should be carefully reassessed by applying a different type of assessment to that required for Article 13.5 and 14 claims, European trade association EHPM has said.

Commenting on the vote today in favour of a list of permitted Article 13.1 claims for use in the European Union (EU), EHPM said that huge issues exist for claims that have not made it onto the permitted list.

The Standing Committee on the Food Chain and Animal Health today adopted the regulation establishing the permitted list of Article 13.1 claims. Claims that will be considered rejected will be included as such in the Union Register and forbidden from use after a six-month transition period.

“Our problem is not with the permitted list of claims, but we remain concerned about claims that have not made it onto this list,” said EHPM Chairman Peter van Doorn. “In addition, some claims have received unfavourable opinions because they were not within the scope of the Nutrition and Health Claims Regulation. However, these should be authorised under the provision of article 10.3 of the regulation allowing reference to general and non specific benefits provided they are accompanied by a specific authorised health claim.”

“Claims that have received negative EFSA opinions should not automatically be considered as rejected,” he continued. “Many of the unfavourable opinions are the result of failures in the procedures, namely a lack of clarity in a number of important issues. We continue to call for further evaluation regarding EFSA’s assessment criteria, which we believe are not appropriate.”

EHPM has consistently called to grade evidence relating to Article 13.1 health claims rather than give yes/no opinions, arguing that both the Nutrition and Health Claims Regulation and the Terms of Reference that EFSA should be following require an assessment of the extent to which cause and effect can be shown.

“The ‘extent’ is determined by the strength, consistency and biological plausibility of the totality of the available data in support of a beneficial nutritional and/or physiological effect,” said Mr van Doorn. “The EFSA pharmaceutical approach does not recognise the complexities of nutrition research and instead opts for the easier route of requiring conclusive cause and effect evidence. EFSA’s only attempt at grading the evidence has been in under one percent of all evaluations, where it stated that there was insufficient evidence to assess the claim.”

ENDS

Notes to Editor:

1. The European Federation of Associations of Health Product Manufacturers (EHPM) was created in 1975, working to provide consumers with safe, science-based, high quality products as well as accurate and helpful information about their nutritional value and use.
2. To contact EHPM email secretariat@ehpm.be, tel: +32 2 209 11 45, or visit www.ehpm.org
Canada

The Natural Health Products Directorate (NHPD) has provided product licence applicants with progressive learning opportunities through online webinars and full day “hands on” workshops to help applicants learn and become proficient with its electronic tools. The NHPD is proud to announce the launch of another innovative learning tool: Instructional Web videos!

The NHPD has created a series of instructional videos on some of the electronic tools offered by the NHPD. The videos are posted on the NHPD website and can be viewed at any time. Each video is approximately 8 minutes in length. These videos give a general overview of each tool. They are meant to demonstrate the ease of use of the tools and help applicants gain familiarity with them.

The videos cover the following topics:

**Natural Health Products Ingredients Database (NHPID)**
- An introduction to the Natural Health Products Ingredient Database, the information it contains, and directions on how to conduct a search.

**Natural Health Products Ingredients Database Issue Form**
- How to fill out the form to have an ingredient or other information added to the NHPID.

**Finished Product Specifications Form**
- An overview of the user friendly FPS form, which helps the user provide quality information quickly and efficiently.

**Electronic Product Licence Application Form (e-PLA)**
- An overview of the electronic product licence application form, and some of its many features.

**e-Submission Builder**
- An overview of the tool that helps applicants package all the necessary supporting documents for their applications which will be submitted electronically to the NHPD.

The videos can be found at the following link:

Energy Drinks

Health Canada's Proposed Approach to Managing Caffeinated Energy Drinks

Help on accessing alternative formats, such as Portable Document Format (PDF), Microsoft Word and PowerPoint (PPT) files, can be obtained in the alternate format help section.

(PDF Version - 204 K)

Background

In recent years, an increasing number of caffeinated beverages have been introduced into the Canadian marketplace. Some of these products are known as "Energy Drinks", which usually contain a range of unique ingredients and may feature health claims related to their capacity to restore energy and alertness. A common substance found in most Energy Drinks is caffeine at levels ranging from those found in a weak cup of coffee to much higher levels. These products also generally contain other ingredients such as vitamins and minerals, and may contain various herbal.

Health Canada has determined, based on consumption patterns, history of use, representation to consumers, and in accordance with its guidance document on "Classification of Products at the Food-Natural Health Product Interface: Products in Food Formats", that products known as Energy Drinks fit the regulatory definition of a food and as such intends to classify these products as foods. As a result, the Department intends to assess, manage the potential risks associated with these products, and regulate their availability in the Canadian marketplace in the context of their use as a beverage.
To Contact:

• Len Monheit, Executive Director, Engredea
  – len@npicenter.com
  – 303-998-9310