

Regulatory Landscape for Botanical Raw Materials

- A U.S. Perspective -

**2016 Korea-China Joint International
Phytonutrient Symposium**

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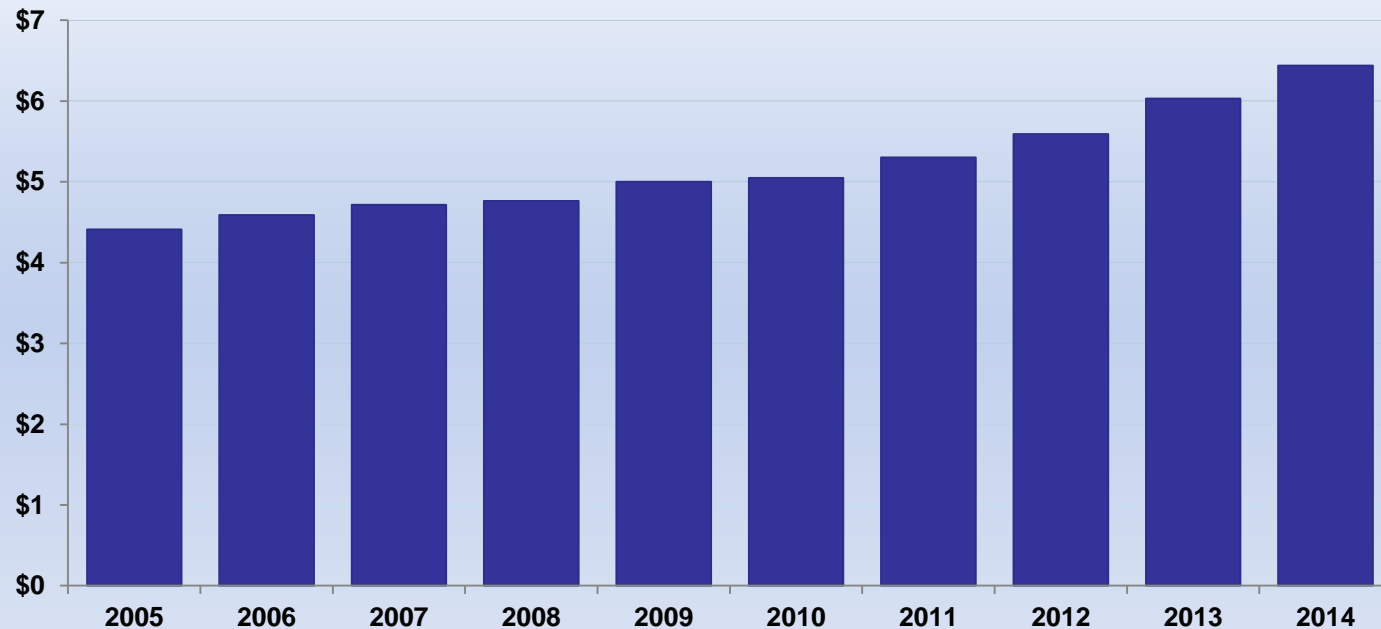
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October 27, 2016

Herbal supplements in U.S.

From *Nutrition Business Journal*

U.S. 10-year HERBAL DS Retail Sales (\$B)



Counting Botanical \$\$\$: U.S.

- **US retail sales of herbal DS in 2014 = \$6.44 B¹**
- **Projecting +8%¹ to +9%² in 2015**
- **Does not include other botanical products:**
 - **Teas in 2014 = \$9.6 B (wholesale)³**
 - **Essential oils > \$1 (or 2?) B annually (retail)**
 - **Kombucha worldwide = \$600 MM⁴ (retail)**
 - **Cosmetics (???)**
- **[By the way: 2014 California almond crop = \$6.46 B⁵]**
 1. NBJ
 2. SPINS 52-weeks to 7/2015; +12.6% for formulas; +1.1% for singles
 3. Tea Association of USA; inc. \$5.2B RTD, \$2.5B “traditional, and \$1.9B “specialty”
 4. BevNet
 5. USDA

Counting Botanical \$\$\$: Int'l

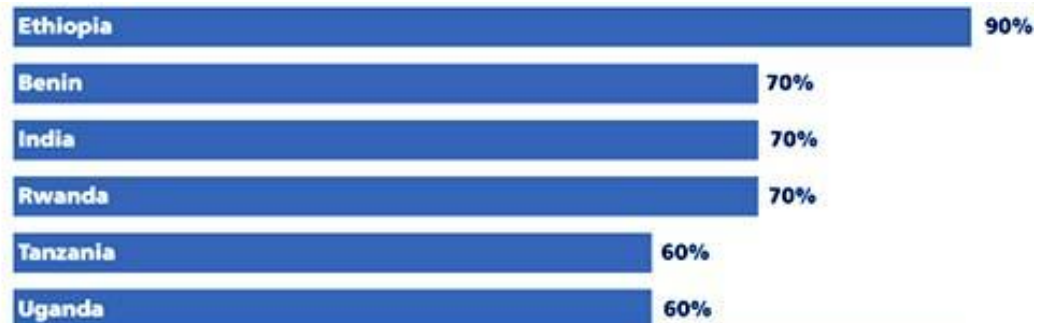
- **China: \$10.8 B in “herbal/traditional products”¹**
- **Global “herbal remedies” market = \$83 B in 2005²**
 - **Excludes soy, algae and fiber**
 - **\$11 B = herbal supplements**
 - **\$14 B = herbal functional foods**
 - **\$14 B = cosmetics/beauty products**
 - **\$44 B = herbal medicines + drugs from herbal precursors**

1. Euromonitor 2015

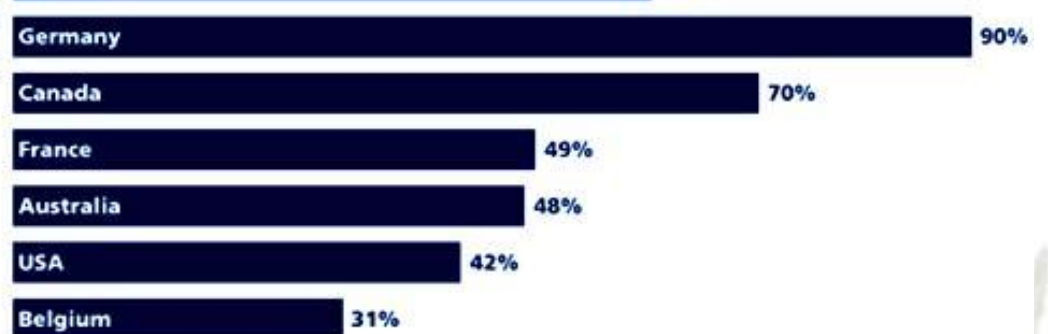
2. Gruenwald 2006

International data

Populations using traditional medicine for primary health care



Populations in developed countries who have used complementary and alternative medicine at least once



WHO Medicines Strategies: National policies on traditional medicine and complementary and alternative medicine. (2004)

Herbs and Botanicals under the U.S. Food, Drug & Cosmetic Act (FDCA)

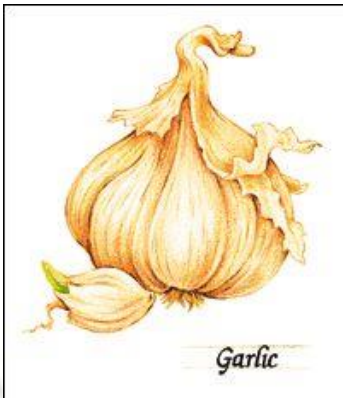


Herbs and the U.S. FDCA

- Under the FDCA, herbs may be used in:
 - Conventional foods
 - Drugs
 - Dietary supplements
 - Cosmetics
- Under the FDCA what is **claimed** for a product (i.e., its “intended use”) and **NOT** its ingredients usually determines its regulatory status

Herbs in foods...

21 U.S.C. 321(f): “The term ‘food’ means articles used for food or drink for man or other animals, chewing gum, and articles used for components of any such article.”



garlic
(*Allium sativum*)



licorice
(*Glycyrriza* spp.)



peppermint
(*Mentha piperita*)

Herbs in drugs... “...diagnosis, cure, mitigation, treatment, or prevention of disease...”

VEREGEN[®]
(sinecatechins) Ointment, 15%

- Rx only since 2006
- Derived from green tea leaf (*Camellia sinensis*)
- Other “botanical drug” (from *Croton lechleri*) approved in 2012

- OTC
- Contains sennosides (*Senna* spp.)



Other OTC herbal ingredients: psyllium seed; slippery elm bark; witchhazel leaf/bark; menthol

Herbs in supplements...



Herbs in foods + supplements

Oats (*Avena sativa*)

FDA authorized health claim: “May reduce the risk of heart disease.”



“...support for stress...”



Herbs in foods + supplements

Garlic (*Allium sativum*)

...essential food ingredient
in many cultures...

“...cardiovascular health”



Herbs in foods + supplements

Licorice (*Glycyrrhiza* spp.)

...for candy and in
beverages, such as teas
and liquors...

... limits set for
glycyrrhizin...



“...benefits and soothes the
stomach...”

...limit on
glycyrrhizin...



Herbs in foods + supplements

Ginger (*Zingiber officinale*)



...in cookies and cakes;
as tea; in many meat &
vegetable recipes...



“...potentiates proper
digestive function.”



Herbs in cosmetics...

21 U.S.C. 321(i) “The term ‘cosmetic’ means articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and articles intended for use as a component of any such articles; except that such term shall not include soap.



**Contains aloe vera gel
(*Aloe vera*)**

Dietary Supplement Current Good Manufacturing Practice (cGMP: 21 CFR 111)

DS cGMP

- Modeled after both food and drug cGMP
- In place since June 2010 (all facilities)
- Key cGMP issues:
 - Basic cleanliness and facility design
 - Adequate training (and documentation)
 - Setting and meeting specifications for identity, purity, strength and composition
 - Written procedures and written records throughout all operations

DS cGMP

21 CFR 111.75(a)(1):

- Before you use a component, you must: (1)(i) Conduct at least one appropriate test or examination to verify the identity of any component that is a dietary ingredient.

21 CFR 111.75(h):

- (1) You must ensure that the tests and examinations that you use to determine whether the specifications are met are appropriate, scientifically valid methods.

DS cGMP

21 CFR 111.75(h):

- (2) The tests and examinations that you use must include at least one of the following:
 - (i) Gross organoleptic analysis;
 - (ii) Macroscopic analysis;
 - (iii) Microscopic analysis;
 - (iv) Chemical analysis; or
 - (v) Other scientifically valid methods

NOTE: FDA does not define the term, “scientifically valid method” in this rule but does record their belief that “a scientifically valid method is one that is accurate, precise, and specific for its intended purpose. In other words, a scientifically valid test is one that consistently does what it is intended to do.”

DS cGMP

21 CFR 111.75(a)(2):

- Confirm the identity of other components and determine whether other applicable component specifications...are met. To do so, you must either:
 - (i) Conduct appropriate tests or examinations; or
 - (ii) Rely on a certificate of analysis from the supplier of the component that you receive [stringent conditions apply]



Best Practices for the Herbal Ingredient Supply Chain

Impacts of FSMA



Food Safety Modernization Act

- ❑ New law passed in 2011
- ❑ “...the most significant overhaul of FDA's oversight of food safety since passage of the Food, Drug, and Cosmetic Act in 1938.”
Congressman Henry Waxman
- ❑ FSMA provides “a risk-based prevention strategy that builds on what the food industry and food safety experts have learned works to prevent harmful contamination and reduce foodborne illness. FSMA recognizes the primary responsibility and capability of those who produce food to make it safe.” **FDA Deputy Commissioner Michael Taylor**
- ❑ Will be implemented over the next several years through seven separate regulations.
- ❑ New 21 CFR 117 is most relevant for botanical ingredients.

21 CFR 117: Organization

- Subpart A: General Provisions
- Subpart B: cGMP (personnel; plant / grounds; sanitation; equipment; processes and controls; warehousing / distribution; defect action levels; etc.)
- Subpart C: Hazard analysis / risk-based prevention controls (written safety plans)
- Subpart D: Modified requirements (defines “qualified facility;” specifies relevant exemptions)
- Subpart E: Withdrawal of qualified facility exemption
- Subpart F: Requirements applying to records
- Subpart G: Supply chain program

21 CFR 117: Affected operations

- ❑ Facilities (U.S. domestic and foreign) that manufacture, process, pack, or hold food for human consumption in the U.S.
- ❑ Exemptions:
 - ❑ Operations now subject to HACCP requirements (fresh juice; fish and fishery products)
 - ❑ Operations now subject to low-acid canned food rule
 - ❑ Dietary supplement makers compliant with 21 CFR 111
 - ❑ Farms in compliance with the FSMA produce safety rule
 - ❑ Certain very small / very low annual sales companies
 - ❑ Low risk on-farm activities
 - ❑ Facilities with only holding operations for certain foods

21 CFR 117 and ingredient controls

- ❑ Current Good Manufacturing Practice, Hazard Analysis, And Risk-based Preventive Controls For Human Food

- ❑ Application to:

- ❑ “Farm mixed-type facilities” (farms that produce foods that are not “produce”)

- ❑ Raw botanical ingredient processors (e.g., cutting, slicing, and other size reduction)

- ❑ Extraction operations

- ❑ Ingredient suppliers (holding operations)

NOTE: The above operations may instead be subject to 21 CFR 111 if its ingredients are “simply packaged” as dietary supplements.

21 CFR 117 and ingredient controls

■ Key requirements:

- Food safety system (written food safety plan); includes hazard analysis and risk-based preventive controls with oversight and management through monitoring, corrective actions, and verification
- Supply-chain programs
 - Required for raw material with identified hazard unless manufacturer controls the hazard with preventive controls.
 - Approved suppliers required (approved by consideration of factors (hazard analysis of the food; ID entity that controls the hazard; supplier performance), or, if from unapproved suppliers: subject to verification activities before being accepted for use.
 - Supplier not required to implement preventive control if hazard is controlled later in supply chain; must label as “not processed to control (identified hazard)” and obtain written assurance from its customer regarding certain actions the customer agrees to take on.

FDA's authority under FSMA

- ❑ Newly expanded records inspection (including personnel training records)
- ❑ Greatly expands ability for administrative detention
- ❑ Mandatory recall authority now established
- ❑ Greater ability to trace products / ingredients to source
- ❑ May suspend facility's FDA registration








Best Practices for the Herbal Ingredient Supply Chain

Voluntary self-regulatory initiatives

GACP: Best Practice Seed to Harvest

Good Agricultural and Collection Practice







GAP: Relevant to farm operations

-  Propagation material (identity; health and cleanliness; purity; organic status; GMO crops)
-  Site selection (fertility; contaminants; location; crop history;
-  Fertilization (choice and identification; application; guidance on both chemical and organic materials (e.g., composted manure)
-  Irrigation (water source and monitoring; irrigation systems; legal conformity)
-  Crop protection and maintenance (cultivation; companion plants; pesticide use)

GACP: Best Practice Seed to Harvest





Good Agricultural and Collection Practice

GCP: Relevant to wild harvest operations

-  Permits and permission (public vs. private property)
-  Site selection (species habitat; site history; proximity to features of concern)
-  Collection equipment (materials; maintenance and cleanliness; training and safety)
-  Identification (training & experience; local floras as resources; voucher specimens; plant's life phase; substitutes and adulterants; positive ID)
-  Sustainability (ESA compliance; abundance; population stability; propagation and regeneration; habitat stewardship)
-  Timing of harvest

GACP: Best Practice Seed to Harvest







Good Agricultural and Collection Practice

-  **General farm standards: Relevant to all operations**
 -  Farm buildings (design; location; light; pest control; order and cleanliness; grounds; waste; etc.)
 -  Farm equipment (suitable; properly functioning; non-toxic construction; clean and well-maintained; adequate toilet and hand-wash facilities; training; etc.)
 -  Farm personnel (food-handling training; safety training; appropriate clothing; absence of disease / wounds; etc.)

GACP: Best Practice Seed to Harvest

Good Agricultural and Collection Practice




Post-harvest handling: Relevant to all operations

-  Handling (containers; avoidance of compaction; protection from contamination; temperature and moisture control)
-  Facilities (light; pest control; order and cleanliness; equipment)
-  Washing and cleaning (water supply; drainage; drying; foreign matter)
-  Dehydration (timing; sunlight and shade; temperature control; air circulation; finished moisture content)
-  Cutting and milling (timing; protection of operators; equipment maintenance; temperature control)
-  Packaging (materials; labeling; storage)

GACP: Best Practice Seed to Harvest







Good Agricultural and Collection Practice

Personnel: Relevant to all operations

-  Training (relevance to tasks; plant identification; hygiene)
-  Safety (clothing; protective gear; environmental factors; tool and equipment)
-  Hygiene (prevention of contamination; toilet facilities; hand washing; personnel health)






GACP: Best Practice Seed to Harvest

Good Agricultural and Collection Practice

-  Record keeping / retentions: For all operations
 -  Agricultural crop harvest records (propagation materials; crop site; agricultural inputs; water source and irrigation; harvest details)
 -  Wild crop collection records (permits and permissions; collection sites; identification procedures; collection details)
 -  Post-harvest handling records (facility; equipment; operations: washing, drying, dehydrating, cutting and milling, packaging)
 -  Personnel records (training; safety and hygiene practices)
 -  Retention samples (representative; labeling; storage; sample correlation at each stage of processing)






Additional Best Practice Farm-gate to Manufacturer

Recommended Practices for Further Handling

-  Special “traditional” preparation (specifications; appropriate traditional references and training)
-  Size reduction (compliance with 21 CFR 117; advance cleaning; timing; protection of operators; dust and temperature controls; metal detection)
-  Extraction (compliance with 21 CFR 117; preparatory steps; solvent selection; post-extraction processing)
-  Packing, packaging and storage (appropriate materials (food grade for contact materials); tamper evidence; protection from light, moisture and humidity, oxygen if required; labeling; away for non-food storage)
-  Shipping (ensure quality to point of delivery; accurate labeling and classification; compliance with transportation rules)

Additional Best Practice Farm-gate to Manufacturer

Recommended Practices for Ingredient Processors

-  Component controls (specifications; lot numbers; labeling; sampling; storage; retention samples; handling of rejects; etc.)
-  Processing operations (MMRs and batch records; duplicate review; confirmation of conformity to specifications; documentation; retention sample; etc.)
-  Laboratory operations (test methods scientifically valid and fit for purpose; qualification of reference materials; etc.)
-  Personnel records (training; safety and hygiene practices)
-  Quality management (appropriate for operation; SOPs and records; system for returns and complaints; quality personnel with significant authority)

THANK YOU!

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American Herbal Products Association

THE VOICE OF THE HERBAL PRODUCTS INDUSTRY