REGULATING "SUPPLEMENTS" FOR A HEALTHY NATION

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OBJECTIVES

- Provide an overview of the Ministry's position on the regulation of "supplements" in Jamaica.
- Update participants regarding status of regulatory framework governing "supplements" locally.
- Briefly indicate challenges faced in regulating the "supplement" Industry.

The best prescription for disease prevention is a healthy lifestyle

INTRODUCTION

WHO Perspectives:

- **Health is a human right**
- **Access to *essential* drugs constitutes part of the human right to health**

Therefore:-

- "Access to *essential* drugs is a human right"

PUBLIC ROLE OF GOVERNMENT

STATE RESPONSIBILITY that protects

- **PUBLIC HEALTH**
- **INTEGRITY OF INDIVIDUAL CHOICE**

REGULATION

Mutual reinforcement of numerous activities all directed at promoting and protecting health. The activities vary from country to country in scope and implementation but usually include common functions.

(WHO, paraphrased)

REGULATION

- **WHO**

  Providers :

  - Health practitioners
  - manufacturers/suppliers of health care products

  Consumers – public education

- **WHAT**

  Products

  - Drugs, foods, supplements, herbal preparations, devices etc.

- **WHERE**

  - Facilities/Institutions
  - Ports of entry

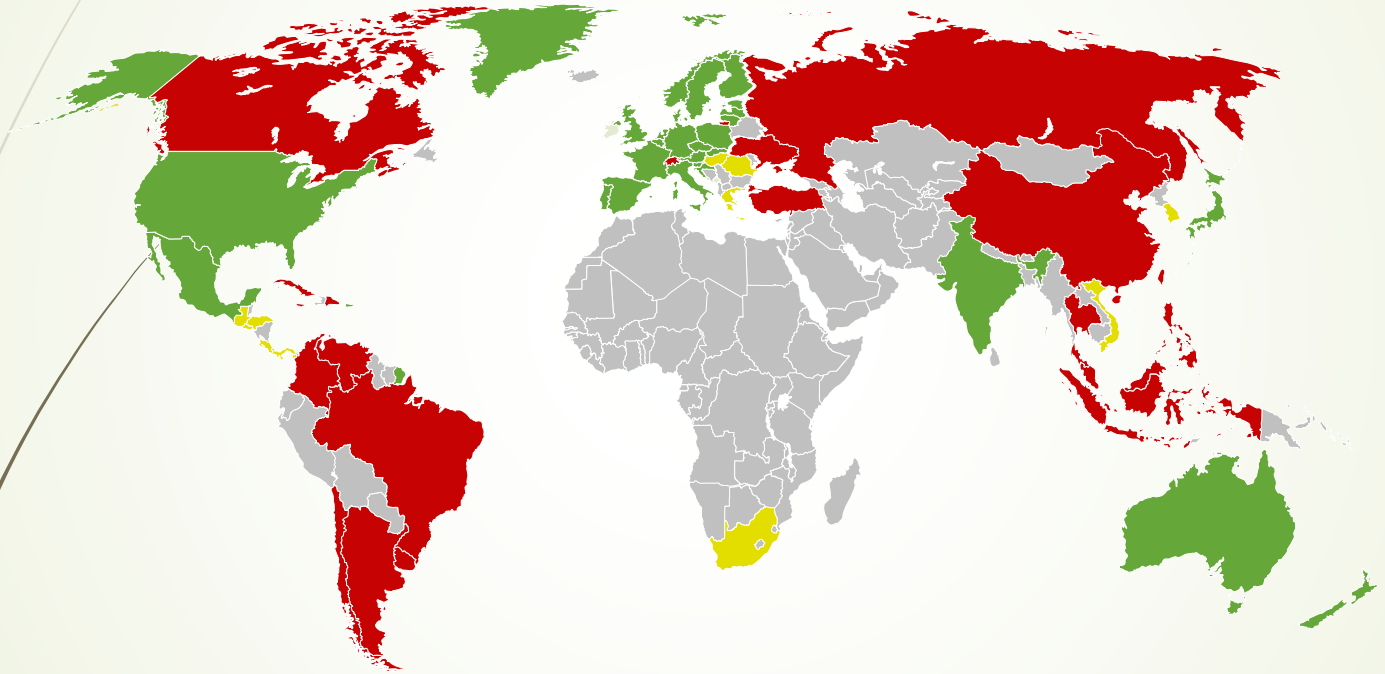
REGULATION

- Sets standards
- Protects people
- Provides redress

- Ensures supply of products and ingredients from reputable sources
- Ensures practitioners take responsible, informed approach regarding safety

Nutrition - Categories Excluding Food Products

(Health Supplements, TCM's, Health Foods and items considered "Drugs/Medicines")



- **Notification or No Registration Market**
- **Registration Market (low/med complexity)**
- **Registration Market (med/high complexity)**

International Regulations

- USA
- Dietary supplements are regulated as "foods" within the meaning of the Dietary Supplement Health and Education Act
- Does not require pre-market notification or registration of products, except for new dietary ingredients
- Prior to DSHEA, FDA tactic was to declare "dubious" supplements as "***unapproved food additives"***
- DSHEA prohibits FDA from doing this
- Since DSHEA, no FDA enforcement jurisdiction unless can prove supplement is "***unsafe***"
  - ***(significant or unreasonable risk of injury)***

International Regulation

- Canada
- Regulatory Authority - The Natural and Non-Prescription Health Products Directorate (NNHPD)
- All products and their manufacturers must be licensed unless the products are made by health care practitioners who compound products on an individual basis for their patients or by retailers of natural health products.

- EU
- Food supplements are regulated as foods, and the legislation focuses on vitamins and minerals used as ingredients of food supplements.
- EU-wide maximum and minimum levels set for each vitamin and mineral
- Companies wishing to market a substance not included in the permitted list need to submit an application to the European Commission

International Regulations

- Australia
- Most dietary supplements are regulated under a category of complementary medicines, which includes vitamin, mineral, herbal, aromatherapy, and homeopathic products
- Complementary medicines may be either listed or registered, depending on their ingredients and the claims made

- China
- Dietary supplements are regulated as health foods.
- The new Chinese Food Safety Law (enacted in 2015) includes 13 items related to health food regulation.
- The China Food and Drug Administration (CFDA) then implemented regulatory system changes, covering the registration and notification processes, creation of a health function claim catalog and an ingredient catalog for health foods, and labeling

Supplement Definition - US

What is a dietary supplement in the US?

- As defined by the United States Congress in the Dietary Supplement Health and Education Act (DSHEA), which became law in 1994, a dietary supplement is a product (other than tobacco) that
  - is intended to supplement the diet;
  - contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and "other substances") or their constituents;
  - is intended to be taken by mouth as a pill, capsule, tablet, or liquid;
  - and is labeled on the front panel as being a dietary supplement.

Supplement Definition: EU

- The European Union – working definition states the following:
- "As an addition to a normal diet, food business operators market food supplements, which are concentrated sources of nutrients (or other substances) with a nutritional or physiological effect. Such food supplements can be marketed in 'dose' form, such as pills, tablets, capsules, liquids in measured doses etc."
- The main EU legislation is Directive 2002/46/EC related to food supplements containing vitamins and minerals.

Supplement: Definition
Food & Drug Act and Regulations - proposed

- "Any product other than tobacco taken by mouth that is intended to supplement the diet, such as, vitamin, mineral, amino acid, enzyme, neutraceutical, dietary substance or concentrate, metabolite, constituent, extract or combination of these ingredients"

INCREASING USE OF DIETARY SUPPLEMENTS

- In 2015, the global market was estimated to be US$109 billion and estimated to grow to US$180 billion by 2020, with the Asia-Pacific, Europe, and North America regional shares at 31%, 30%, and 25%, respectively.
- Another projection for the global market was US$278 billion by 2024.
- The range and composition of dietary supplements are almost endless
  - common multivitamins are packaged for specific groups by age, gender, physical conditions, and activity level

Driving forces

Several factors contribute to the increasing use of dietary supplements:

- An aging baby boomer population, with concerns for wellness, fitness, and enhanced quality of life;
- Increasing use of natural substances, while rejecting the so-called chemicals; alternative therapies and natural remedies - (Wholistic Medicine)
- Increasing cost of drugs and a suspicion that drug companies have ignored "natural" products because their use could not be protected by patents
- A willingness to "try anything" in the search for a cure for a chronic disease

Driving forces contd.

- Continuous introduction of novel preparations
- notion that "natural" is synonymous with safe
  (free from adverse/harmful effects)
- Marketing of dietary supplements has expanded
  - Many thousands of products are advertised as being beneficial for health, disease prevention, or even enhancement of mental or physical performance.
- Sufficient evidence exists for benefits – in some cases
  - no significant value over carefully "planned and balanced diet'
- Basis for regulation established

Concerns

- As the use of dietary supplements has increased, the number of liver injuries reported as complications of their use has also increased, and these complications are usually dose related.
- Commonly implicated agents include anabolic steroids used for body building, green tea extract, and multi-ingredient nutritional supplements.
- Increasing use of dietary supplements raises public health concerns about their efficacy and safety in both short and long terms and demands a public health approach to their regulation.

Drug

Regulated as a drug

Dietary supplement

Also regulated

Regulated as a

What ?

Natural Health Product

Comparing Pharmaceuticals, Dietary Supplements

Pharmaceuticals

- Chemical can be natural or synthetically derived
- Regulates as drugs
- Requires regulatory pre-market assessment of risk, efficacy
- Post-marketing surveillance (for adverse reactions)
- System is not perfect
- Some risks not identified until after marketing

Dietary Supplements

- Chemical is derived from foods plant or animal tissues
- *Generally,* **natural** chemicals
- Regulates as **foods/ nutritional products**
- Pre-market assessment of risk is limited
- No assessment of efficacy
- System is not perfect
- Some risks not identified until after marketing
- Some risks differ from pharmaceuticals

LEGISLATIVE FRAMEWORK

- **FOOD AND DRUGS ACT 1964 & REGULATIONS 1975**
- **PHARMACY ACT 1966 & REGULATIONS 1975**

SCOPE

- **Food – " any article used for food or drink by man, including chewing gum and any ingredient that may be mixed with food or drink for any purpose"**

- **Drug – "any substance or mixture of substance manufactured, sold or represented for use in -**
  - The diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state or the symptoms thereof in man or animal;
  - Restoring, correcting or modifying organic functions in man or animal;

Why Continue to Regulate Products of Natural Origin

- Protect product integrity-
- Protect consumer interests– product claims
- Maintain requisite standards – batch to batch consistency
- Ensure public safety not compromised – toxicities
  - Products, practices lead to positive clinical outcomes, improved quality of life
    - safe,
    - effective,
    - good quality

Product Integrity-

- **QUALITY**:
  - Conformity assessment for proper identity
  - Content verification
  - Impurities/contaminants
    - **Heavy metals, aflatoxins, moisture**
    - **Synthetic material added**?
  - Raw materials – source, processing, etc.
  - GMP, GAP
  - Product stability – studies conducted under the appropriate conditions

Common problems noted

- Misrepresentation of product contents.
- Different recommended dosages among products.
- Inadequate information about how a company's herbs are grown and processed.
- Poor standards of quality, product safety, or activity of ingredients.
- **As a result:** governments and industries are working to develop high-quality manufacturing guidelines Good Manufacturing Practices (GMP) for all dietary supplements, including botanical products.

Quality Standard Differences

- Drug
  - Utilize Pharm Good Manufacturing practices (GMP)
  - Main focus on consistency, potency and purity.

- DS/Foods
  - Utilize Food (GMP)
  - Main focus on the reduction of contaminants adulterants and filth.

Good Manufacturing Practices (GMPs)

Good Manufacturing Practices for supplements must cover:

product specifications, premises, equipment, personnel, sanitation program, operations, quality assurance, stability, records, batch samples, and recall reporting

Integrity contd.

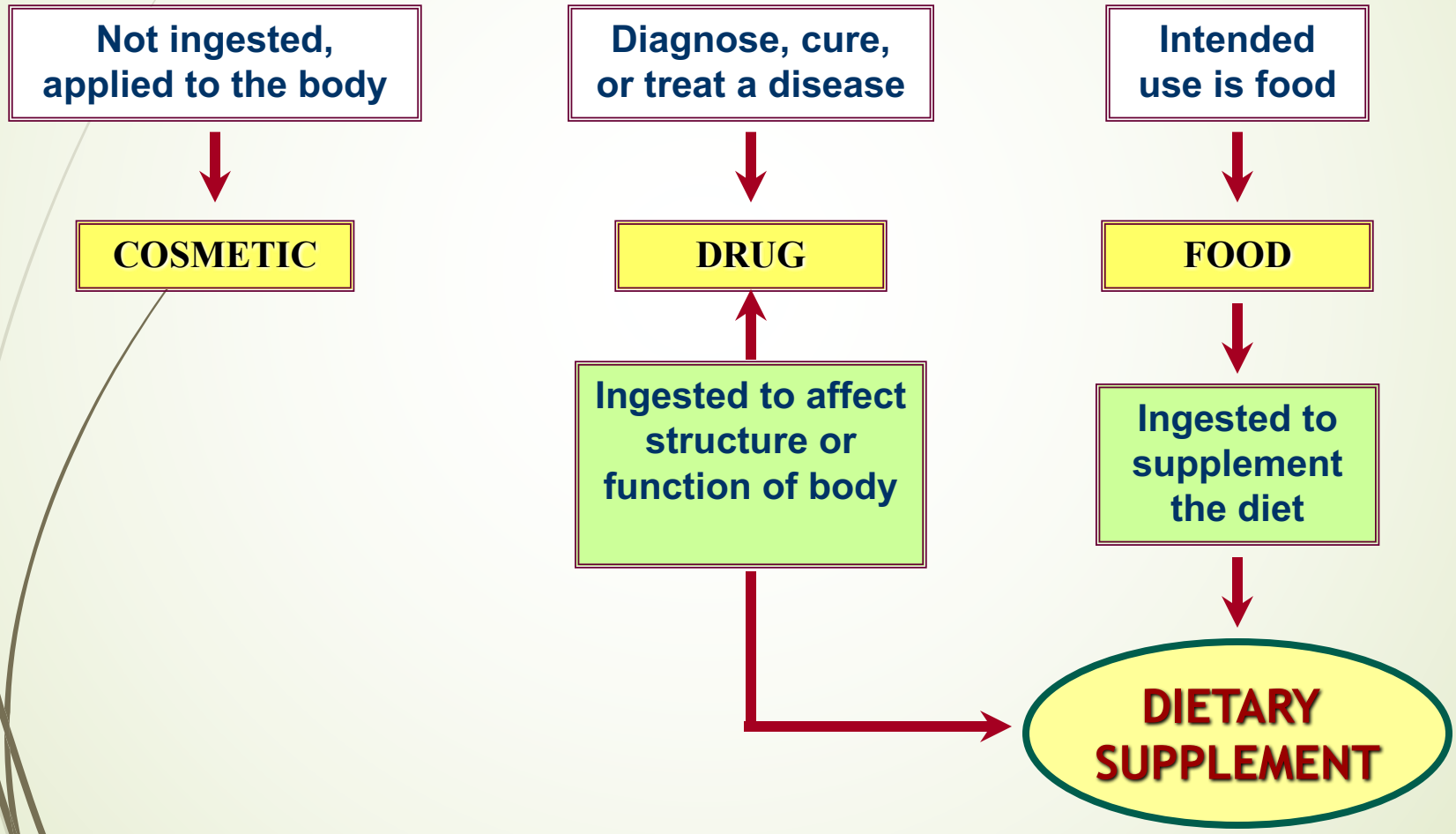
- EFFICACY
  - Ability to effect label claim - indication/action
  - Pharmacological activity
  - Potency - justification for effective dose
  - Rationale for combination therapy – combination products a matter of concern
  - Nature of claims - justification

Dietary Supplement

Food

Drug

"Intended" Use Makes a Difference



Drugs vs. Dietary Supplement Claims

- Drug manufacturers may claim that their product will diagnose, cure, mitigate, treat or prevent a disease.

- Dietary supplement manufacturers cannot legally make these claims!

What can dietary supplement manufacturers claim?

- A dietary supplement or food product may contain one of **three** types of claims:
  - **A health claim** - "diets high in calcium may reduce the risk of osteoporosis";

    "Maintains healthy circular system"
  - **A nutrient content claim** - "A good source of …"
  - or **A structure/function claim** - "calcium builds strong bones.", "antioxidants maintain cell integrity";

    "for muscle enhancement"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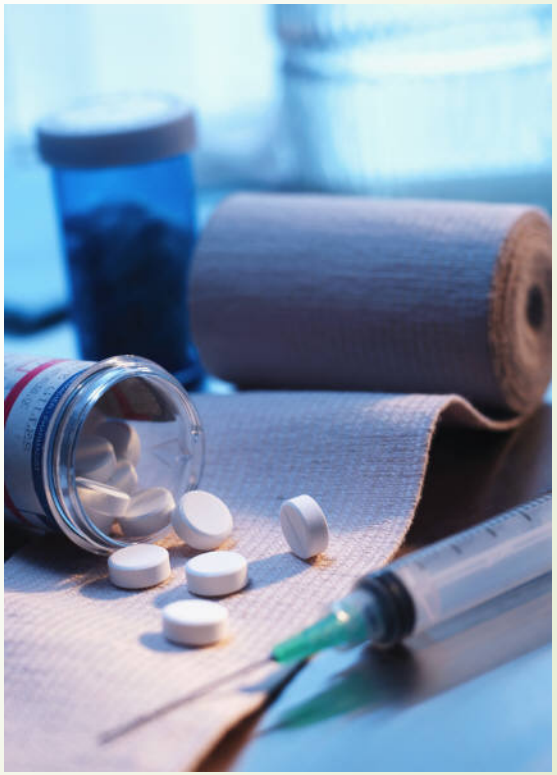
Integrity contd.

- SAFETY
  - Toxicity
    - Acute
    - Long-term
    - Mild, severe
  - Reporting responsibility
  - Interactions, contraindications
  - Use in children

Safety categorization plays a major role!

Food <<<<<<<<<<<<<<>>>>>>>>>>>>>>Drugs



Safety Assumptions

- Drugs - Health benefit vs. risk evaluation.
- Generally regarded as unsafe!

- Dietary supplements - Components are Generally Recognized as Safe

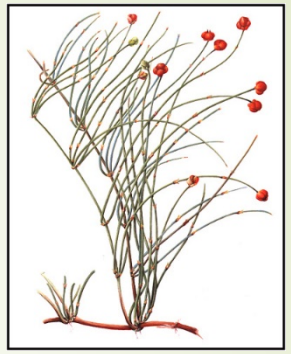
Adverse Events Associated with Supplements: Examples

- L-tryptophan and eosinophilia-myalgia syndrome
  - 1989: 1500 cases, 27 deaths attributed to contaminant in manufacturing process at a single facility in Japan
- Other examples of supplements containing unwanted addition of undesirable contaminants
  - Digitalis poisoning resulting from plantain-derived dietary supplement contaminated by digitalis lantana
  - Studies have identified other environmental contaminants in dietary supplements
    - Aflatoxins, lead, mercury, DDT as examples

Adverse Events Associated with Dietary Supplements: Examples

- Some dietary supplements may interact with effects of pharmaceutical drugs
- St John's Wort
  - Can induce as well as inhibit liver enzymes involved in the metabolism of drugs and other chemicals
    - Cyclosporin
    - Indinavir
    - Oral contraceptives
    - Tricyclic antidepressants
    - Benzodiazepenes

Other Dietary Supplements of Current Concern



- Plant alkaloids containing ephedrine
  - Example of botanical: Ma Huang (*ephedra sinica*)
  - Contains mixture of mainly ephedrine, other stimulant alkaloids
    - Pseudoephedrine (common OTC decongestant)
- Widely marketed as dietary supplement
  - Weight loss, athletic enhancement
- Pharmacology, toxicology of ephedrine, related alkaloids
  - Increased heart rate, blood pressure (blood vessel constriction), bronchodilator effects
- Some studies have demonstrated poor correlation between product labeling and actual dose of what appears in the product
  - Contrast with regulatory oversight over pharmaceuticals
    - Good Manufacturing Practices (GMP's)

Restricted herbs: considered toxic, and given their side effects, should be avoided

- **Chapparal:** irreversible liver damage.
- **Comfrey:** liver toxicity, carcinogenic effects, and damage to fetus if used during pregnancy.
- **Ephedra:** hypertension, myocardial infarction (MI), seizure, stroke, psychosis. 155 deaths and over 16,000 side effects.
- **Germander:** liver damage and death.
- **Kava:** liver damage, especially risky for those with liver problems.
- **Lobelia:** breathing problems, rapid heartbeat, low blood pressure, coma, or death.
- **Willow bark**: Reye's syndrome in children, and allergic reaction in adults.
- **Wormwood:** seizures, numbness of legs and arms, delirium, and kidney failure.
- **Yohimbe:** hypotension (low blood pressure), heart conduction disorders, kidney disorders, nervous system disorders, death.

Regulatory Requirements

- Result of consultative process:
  - MOH, Wholistic Herbal Assoc.,
  - Open fora with Select Committee on Human Resources & Social Development
- Reference by MOH to legal approach taken by Competent Authorities in Australia, Canada, Germany, England, United States, others.
- Reference to WHO Guidelines on the Assessment of Herbal Products. Definitions adapted - in use.

Present Regulatory Framework

- Recommendations based on collaborative work.
- Product classification scheme identified, presently used.
- Food & Drug Act to be amended
- Regulations being developed
- Advisory Panel Mechanism for Complimentary Medicines to be re-established,
- Food Advisory Committee established 2006, October

Scope of Amendment to F&D Act

- **Natural Health Products Division**
- **New categories of substances:**
  - **Herbs**
  - **Herbal Materials**
  - **Herbal Remedies**
  - **Finished Herbal Products**
  - **Health Foods to include dietary supplements and Neutraceuticals**
- **Drugs, Foods - status remain unchanged**

Herbs:

Include plant material e.g. leaves, flowers, seeds, fruit, stems, wood, bark, roots, rhizomes or other plant parts ,which may be entire, fragmented or powdered.

Herbal Material:

Include in addition to herbs, fresh juices, gums, fixed oils, essential oils, resins, dry powders of herbs.

Herbal Remedy:

Any botanical product consisting of a substance produced by subjecting a plant /plants to drying, crushing or any other process or mixture whose sole ingredients are two or more substances so produced.

May have potential to be used for risk reduction, therapeutic or treatment purposes. Include traditionally used and new ones.

Health food:

"Any product other than tobacco taken by mouth that is intended to supplement the diet, such as, vitamin, mineral, amino acid, enzyme, neutraceutical, dietary substance or concentrate, metabolite, constituent, extract or combination of these ingredients"

Requirements for Registration- Natural Health Products

- Statement of content
  - **Concentration, source, dose**
- Posology
- Rationale for combinations
- Toxic/side effects
- Tests to confirm quality, potency
- Verification of label claim
  - **Clinical trials, data or references to published studies, journals, pharmacopoeias, and traditional resources**
- Approval in country of origin
- Scientific support of shelf life
- Samples
- Fee
- Other pertinent information

Note:

- All products regulated except
  - Homeopathic preparations more dilute than a one thousand fold dilution of a mother tincture.
  - Herbal teas except where there are claims.
  - Products which exist and function principally as food if they make no therapeutic claims e.g. garlic
- Fees required for passive assessment
- All injectable presentations registered as prescription drugs

CHALLENGES

- Public Perception remains unchanged
- Regulatory intervention
- Gap in public education programmes
- Insufficient information for many herbs presents barrier to proper scientific review
- Inadequate laboratory support
- requisite documentation often not supplied

Challenges

- Many supplements contain multiple ingredients, change composition over time, or are used intermittently at doses difficult to measure.
- It may take a long time for the current systems of voluntary adverse event reporting to detect public health problems associated with inappropriate supplement use.

Expectations:

- Maximum benefits to the consumer
- No double standards in quality
- Honest communication to the public
- Public health & safety not compromised

The best prescription for disease prevention is a healthy lifestyle

References

- Abrams SA. 2015. Is it time to put a moratorium on new infant formulas that are not adequately investigated? J. Pediatr. 166:756–60
- Ackatia-Armah RS, McDonald CM, Doumbia S, Erhardt JG, Hamer DH, Brown KH. 2015. Malian children with moderate acute malnutrition who are treated with lipid-based dietary supplements have greaterweightgainsandrecoveryratesthanthosetreatedwithlocallyproducedcereal-legumeproducts: a community-based, cluster-randomized trial. Am. J. Clin. Nutr. 101:632–45
- AlbertBB,DerraikJGB,Cameron-SmithD,HofmanPL,TumanovS,etal.2015.Fishoilsupplements in New Zealand are highly oxidised and do not meet label content of n-3 PUFA. Sci. Rep. 5:7928
- AlbertBB,DerraikJGB,GargML,Cameron-SmithD,CutfieldWS.2017.Concernswiththestudyon Australian and New Zealand fish oil products by Nichols et al. (Nutrients 2016, 8, 703). Nutrients 9:137
- Anderson JJB, Kruszka B, Delaney JAC, He K, Burke GL, et al. 2016. Calcium intake from diet and supplementsandtheriskofcoronaryarterycalcificationanditsprogressionamongolderadults: 10-year follow-up of the Multi-Ethnic Study of Atherosclerosis (MESA). J. Am. Heart Assoc. 5:e003815
- Andrews KW, Roseland JM, Gusev PA, Palachuvattil J, Dang PT, et al. 2017. Analytical ingredient content and variability of adult multivitamin/mineral products: national estimates for the Dietary Supplement Ingredient Database. Am. J. Clin. Nutr. 105:526–39

References

- FAO (Food Agric. Organ.). 2017. The Codex Alimentarius international food standards. Updated Sept. 20, FAO, Rome. http://www.fao.org/fao-who-codexalimentarius/en/
- FerrucciLM,BellBP,DhotreKB,ManosMM,TerraultNA,etal.2010.Complementaryandalternative medicine use in chronic liver disease patients. J. Clin. Gastroenterol. 44:e40–45
- Food Stand. Aust. N. Z. 2016. Food for special medical purposes. Updated June, Food Stand. Aust. N. Z., Canberra. http://www.foodstandards.gov.au/consumer/nutrition/foodspecial/Pages/default.aspx
- Food Stand. Aust. N. Z. 2016. Food standards code. Food Stand. Aust. N. Z., Canberra. http://www. foodstandards.gov.au/code/Pages/default.aspx
- Frank LL. 2015. Thiamin in clinical practice. J. Parenter. Enteral Nutr. 39:503–20

References

- TGA (Ther. Goods Adm.). 2016. Australian Regulatory Guidelines for Complementary Medicines. Canberra: TGA, Aust. Gov. Dep. Health. https://www.tga.gov.au/publication/australian-regulatoryguidelines-complementary-medicines-argcm
- TGA (Ther. Goods Adm.). 2016. Complementary medicines. TGA, Aust. Gov. Dep. Health, Canberra. https://www.tga.gov.au/complementary-medicines
- UNICEF.2015.ManagementofSevereAcuteMalnutritioninChildren.UNICEFProgr.Guid.Doc.New York:UNICEF.https://www.unicef.org/eapro/UNICEF_program_guidance_on_manangement_of_SAM_2015.pdf
- US FDA (Food Drug Adm.). 2009. Warning on Hydroxycut products. Updated May 1. US FDA, Silver Spring, MD. https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm152152.htm
- US FDA (Food Drug Adm.). 2015. Responses to questions about Codex and dietary supplements. Updated July 9. US FDA, Silver Spring, MD. https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/DietarySupplements/ucm113860.htm
- USFDA(FoodDrugAdm.).2017.Dietarysupplementproductsandingredients.UpdatedAug.1.USFDA, Silver Spring, MD. https://www.fda.gov/Food/DietarySupplements/ProductsIngredients/
- USFDA(FoodDrugAdm.).2017.Whatisadietarysupplement.UpdatedJan.13.USFDA,SilverSpring, MD. https://www.fda.gov/food/dietarysupplements/usingdietarysupplements/ucm480069.htm#what_is