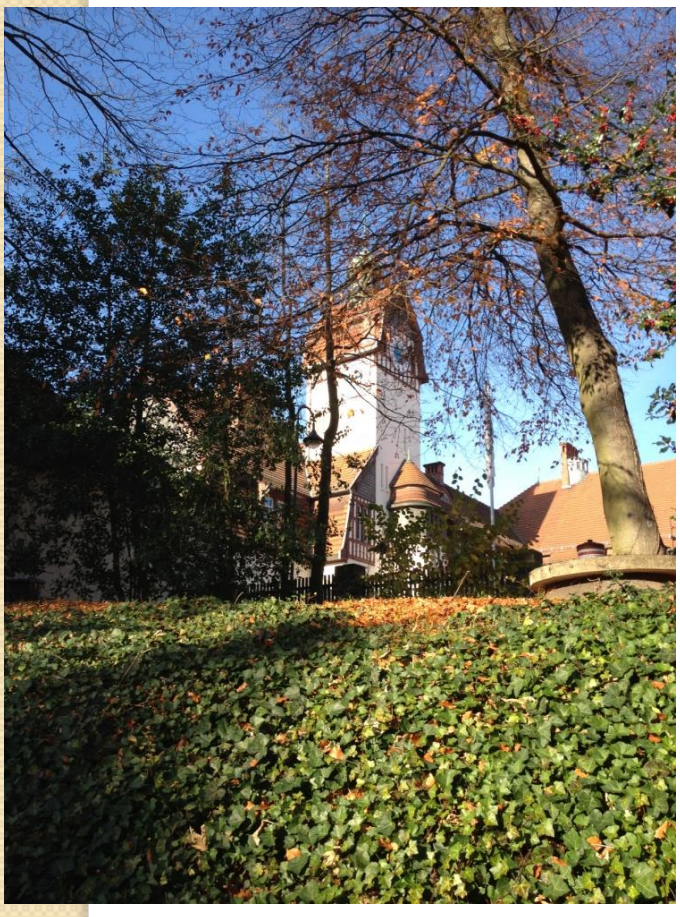
CRNI – Supporting Science Based Regulation on a Global Scale



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A quality dietary supplement: before you start and after it's marketed – a conference report – EJN Supplement

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- Conference Observations from Brisbane, Australia
- A Year On – What has Changed?
- Supply Chain Oversight
- Establishing the FSMA model of HAACP requirements for raw material purveyors
- Evaluating international models
- Consumer Protection – The Ultimate Goal

Conference Conclusions

(1) Quality is a noun describing "how good or bad something is."

(2) Quality is a noun describing "a characteristic or feature that someone or something has; something that can be noticed as a part of a person or thing."

(3) Quality is a noun describing "a high level of value or excellence."

- In summary, the "quality" of a dietary supplement of nutritional product can either be "good" or "bad," objectively measured via analytical parameters.
- Dietary supplements and nutritional products have an inherent "quality," i.e., a feature that is descriptive of the product as desired, purchased and used.
- Finally, a "quality" dietary supplement and nutritional product is one with a high level of value or excellence…it is the product the consumer wants.

Good Manufacturing Practices (GMP's)

- There are GMP requirements specific to the *safety and quality* of a product related to the manufacturing, packaging and labeling for all foods, dietary supplements and pharmaceutical products.
- CRNI believes Codex should promote *harmonization* internationally on key attributes.

GMP's – The Hallmark of Integrity

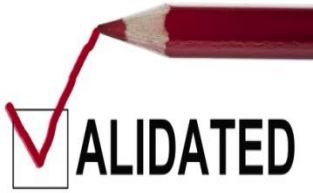
- The *process control approaches* to ensure safety and quality assurance, such as quality verification and validation of the product and process are raised or highly recommended by GMP regulation or international quality management schemes.

US-GMP Framework (21 CFR 111)

- The US model for GMP regulations is unique, and although specific for the manufacturing of dietary supplements, it is in reality a *hybrid of food and pharmaceutical GMPs*. The dietary supplement regulations define the manufacturing and quality requirements for all supplements sold and distributed in the US market.

Verification and Validation

- There is confusion with the terms "verification" and "validation," and any distinction is not overly apparent to some manufacturers or auditors.
- In the manufacturing chain for dietary supplements, supplier control and the examination or testing of raw materials per the specifications for production is normally considered to be one of the most critical points to control as any deviation would drastically impact product quality including the identity, strength, composition and any potential contaminants.



Key Challenges Globally

- Economic Adulteration remains a critical concern in the supply chain – particularly in a global marketplace.
- The illegal inclusion of Undisclosed Active Pharmaceutical Ingredients (UAPI's) within 'herbal' compounds is likewise a growing problem.

Key Challenges Globally

- Supply Chain Traceability is Mission Critical
- Verification of Certificate of Analysis data by subsequent testing is a critical component of a rational GMP system
- Physical Audits of foreign facilities presents economic and scheduling challenges but should be promoted by responsible Codex bodies such as CCNFSDU.

Supplier Compliance – A Global Perspective

- Any supplier who has the potential to impact product quality should be managed in a structured way to minimize risk to product quality. The supplier compliance management process is made up of three main elements:

  (1) approving a potential supplier;

  (2) monitoring performance, followed by

  (3) periodic on-site reviews.

The Scope and Value of GMP Audits

- A quality GMP audit is defined as a systematic, independent and documented process to examine specific activities relating to the physical environment, systems and processes which impact the product.
- CRNI believes that Codex can play a significant role in espousing this approach on a global basis.

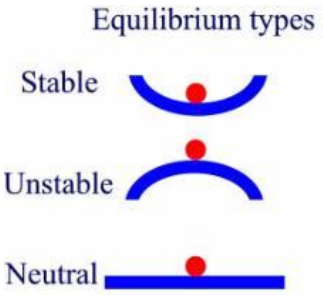
Beware of Inappropriate Testing

- In the US recently several products involving herbal extracts were tested for DNA signature. Conclusions were drawn which may clearly be incorrect.
- This test may be appropriate for raw botanicals, but has little merit in evaluation of extracted compounds where little if any residue of the baseline product genus and species should be present.

Stability and Shelf Life – a Key Consumer Concern

- Owing to their similarities in presentation, there is a tendency for government authorities to consider that all requirements for medicines are equally applicable to supplements, and this includes the issue of stability testing.
- For medicines, stability is essentially a safety concern, as stability testing ensures the safety and consistency of delivery of the drug over time.

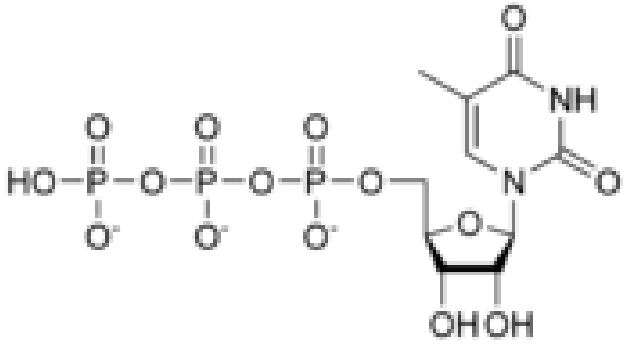
Supplement Stability



- The essential requirements of supplement stability are to ensure that no untoward organoleptic changes take place during the proposed life of the product and also to ensure that the product meets the quantitative requirements for the claimed active ingredients throughout its proposed shelf life.
- This is clearly a different paradigm than pharmaceuticals and Codex needs to embrace this approach for the benefit of the consumer.

Post-Market Surveillance

- One of the most frequent criticisms of dietary supplement regulations and basis for scrutiny around the safety of such products is that there is often no pre-market clinical testing required which would have required that preliminary safety assessments be conducted.



Post-Market Surveillance

- It is important to acknowledge certain deficiencies which are common to any pre-market analysis (for drugs or dietary supplements) including sample populations which are not an accurate representation of the population at large and therefore may not account for relevant factors which can affect the expectedness of certain events or outcomes.

Post-Market Surveillance

- Future considerations in post-market safety surveillance for dietary supplements include developing standardized/ globally accepted causality assessment criteria which is specific to complex substances (i.e., multi-ingredient dietary supplements) to reduce generalization which contributes to inaccurate conclusions regarding the safety of supplements and/or their ingredients.

CRNI – The Global Leader in Scientific Symposia for the Dietary Supplement Industry

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