The scope of dietary ingredients under DSHEA: Synthetic copies of botanical constituents

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FDA Public Meeting: Responsible Innovation in Dietary Supplements
Center for Food Safety and Applied Nutrition
College Park, MD
May 16, 2019

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Presentation Outline

1. FDA's goals and public health importance of the NDI Guidance (August 2016 draft)

2. DSHEA negotiation notes regarding new synthetic ingredients

3. The synthetic botanical ban: when and why?

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4. Congressional and industry response to this synthetic botanical policy

5. Current issues and market realities

6. Recommendations to FDA

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FDA's goals and public health importance of the NDI Guidance (Aug 2016 draft)

1. The NDI process is the sole pre-market opportunity to assess the safety of new dietary ingredients
2. To improve the rate of NDIN compliance
3. To improve the quality of NDIN notifications
4. NDINs serve as a preventive control to assure consumers are not exposed to unnecessary public health risks in the form of new ingredients of unknown safety

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FDA's rationale for excluding synthetic botanicals

- A synbot's status is defined by its nutritional function, not by its state of matter (e.g., botanical).
- A substance that has been synthesized in a lab or factory has never been part of an herb or other botanical, therefore it is not a dietary ingredient.
- Synbots were not part of the human diet and therefore cannot increase the "total dietary intake" of something not part of the human diet.

- This rationale dates back to 2001 and is a result of FDA's final rule declaring dietary supplements containing ephedrine alkaloids adulterated *(see page 39, footnote 33, FDA New Dietary Ingredient Guidance for Industry, August 2016)*.

- So, FDA's synthetic botanical policy was developed to deal with a pre-DSHEA issue and finally resolved by regulation in 2004.

United States Senate
WASHINGTON, DC 20510

December 22, 2011

Margaret Hamburg, M.D.
Commissioner of Food and Drugs
Food and Drug Administration
109903 New Hampshire Ave.
Building 1, Room 2217
Silver Spring, MD 20993

Dear Commissioner Hamburg:

As the principle authors of the Dietary Supplement Health and Education Act of 1994 (DSHEA), we write to express our significant concern regarding the Food and Drug Administration's (FDA) draft guidance for industry entitled, "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues," which the agency published on July 5, 2011. For the reasons outlined below, we urge the FDA to withdraw this guidance and begin work on a new draft that will provide needed clarification on what constitutes a New Dietary Ingredient (NDI), but does not undermine the balance Congress struck in DSHEA to provide consumers with access to safe, affordable dietary supplement products.

When Congress included language in the Food Safety Modernization Act (FSMA) directing FDA to clarify when a dietary supplement ingredient is a new dietary ingredient, the expectation was that the guidance would be consistent with DSHEA. Unfortunately, the draft guidance serves to undermine DSHEA in a number of important respects.

For example, the draft guidance would require a manufacturer to submit an NDI notification for every dietary supplement containing an NDI. This is directly contrary to the language of DSHEA, which requires notification only of the intent to use an NDI. The FDA's misinterpretation of this provision is far from harmless. Indeed, this burdensome requirement would impose substantial, additional costs on manufacturers without providing additional safety benefits, and would undermine the access to safe, affordable dietary supplement products that DSHEA was designed to ensure. Similarly, the draft guidance attempts to assert that synthetic copies of botanicals can never be a dietary ingredient, an assertion that is wholly without statutory basis, and in fact contradicts longstanding FDA policy. The draft guidance also unduly limits the types of physical modifications that do not result in "chemically altering" a dietary ingredient by incorrectly construing the list in DSHEA legislative history as an exclusive rather than illustrative list. Furthermore, it diverges from our intent by including only ingredients that were marketed before enactment of DSHEA in the form of dietary supplements as "old dietary ingredients." The term dietary supplement wasn't even defined prior to DSHEA.

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"Similarly, the draft guidance attempts to assert that synthetic copies of botanicals can never be a dietary ingredient, an assertion that is wholly without statutory basis, and in fact contradicts longstanding FDA policy."

Because of these and other concerns, we urge FDA to immediately withdraw this guidance and start the process of crafting a new document that addresses these and other concerns. As part of that process, we would ask that you direct your staff to sit down with our staff early in January to discuss these concerns in more detail.

Thank you for your attention to this matter. We look forward to your prompt reply. If you have any questions, please have your staff contact Jenelle Krishnamoorthy with Senator Harkin and Hayden Rhudy with Senator Hatch.

Sincerely,

Tom Harkin
U.S. Senator

Orrin G. Hatch
U.S. Senator

Cc: Jeanne Ireland

2019 realities

- Synthetic chemistry, synthetic biology and synthetic botanicals have evolved dramatically since 1994.
- They are currently and will continue to enter the food, ingredient, spice, color, flavor and dietary ingredient sectors.

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evolva

Evolva – a yeast "metro" for valuable products

Ambergris

Pyrethrin

Caffeine

Opiates

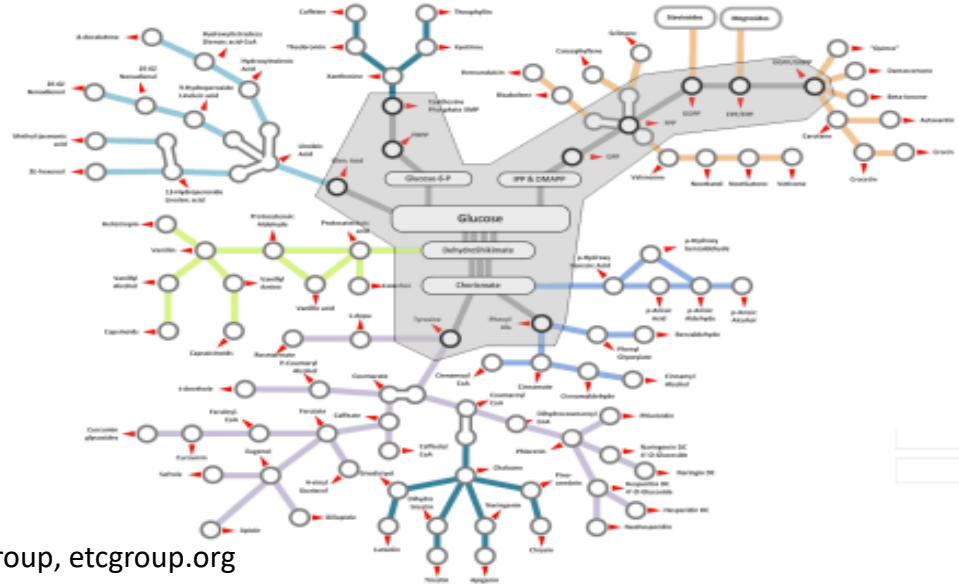
Cocoa

Sandalwood

Stevia

Saffron

Musk



Frankincense

Caviar

Mint

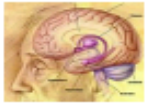
Capsiate

Source: ETC Group, etcgroup.org

Taxol

Vanilla

Dopamine



Resveratrol

Turmeric

Carmine

Breast Milk

Ginseng

Truffles

Economic Disruption

- Synthetic botanical ingredients are often far less expensive than natural counterparts and are used to spike up or top up botanical extracts.
- Analytical detection is often difficult.
- Raw material pricing becomes skewed as synbots are added to or replace botanical ingredients or extracts. This encourages economic adulteration, misbranding, mislabeling and consumer deception.

Presence of Synthetic Curcumin

- C14 testing is required to detect the presence of synthetic curcumin
  - Testing is quantitative
- If adulterated, typical range of material is between 5 and 16%
- Net impact on raw material costs can be between 10 and 20%, translates to 50 to 70% on retail (online) prices
  - >40 % of samples tested (online purchases) contain some synthetic curcumin

Synthetic Curcumin Detection

Global Curcumin ASSOCIATION

Lot#	Expiration Date	Curcumin label claim (mg/cap)	#Caps/SG	Capsule/ Softgel	Natural vs. Syn
B-851	Aug-21	1350mg/150mg	90	Veg Caps	100%
6098901	Mar-20	500 mg	180	Capsule	100%
197170	Jun-20	1100mg	60	Capsules	100%
000002	Jun-19	500 mg	180	Capsules	92%
3052806	Apr-21	665/630 mg	60	Veg Caps	100%
704056	Mar-19	1650 mg	90	Veg Caps	95%
221307	Jan-22	300 mg	60	Veg Caps	100%
800002	Apr-20	500 mg	240	Capsule	86%
299279-05	Jun-22	500 mg	90	Capsules	100%
2018-04381	22-Jan	100mg	60	Veg Caps	90%
1833196	20-Nov		90	Tablet	84%
8071771	20-Oct	400 mg	65	Capsules	100%
11196-120	20-Jan	1950 mg	120	Veg Caps	89%

Summary

- Synthetic botanicals are a growing percent of the botanical dietary supplement market.
- FDA's current synthetic botanical NDIN policy is inconsistent with the mission statements of the 2016 NDI guidance and the intent of DSHEA.

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- The genesis of the current synthetic botanical policy was to remove synthetic ephedrine alkaloids as dietary ingredients.

- The continued use of this 2004 final regulation on ephedrine alkaloids as the basis for the current synthetic botanical policy is unhelpful.

Recommendations to FDA

Revise the “no synthetic botanicals as NDI” policy as follows:

- Recognize synthetic copies of botanicals as new dietary ingredients subject to notification.
- Require label declaration of the presence of a synthetic botanical on label and labeling of dietary supplements.

- Treat non-NDI compliant synthetic botanicals as unlawful dietary ingredients.

- Seek public comment on the use of GRAS affirmation as the basis to establish safety of synthetic botanicals with respect to NDI status.

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Thank you!

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