

United States Senate

SPECIAL COMMITTEE ON AGING

WASHINGTON, DC 20510-6400

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December 12, 2016

The Honorable Robert M. Califf, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: Comments on Proposed Draft Guidance Titled: “Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry”

Dear Dr. Califf,

I write to provide comments on the recently released draft guidance entitled, “Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry.”

Under the Dietary Supplement Health and Safety Act of 1994 (DSHEA), the new dietary ingredient (NDI) notification process represents one of the few pre-market notifications FDA receives before a dietary supplement manufacturer introduces a new product to the market. Dietary supplement manufacturers wishing to use an NDI—a dietary ingredient not on the market before October 15, 1994—in a product must notify FDA of their intention, and provide safety and history of use information for the ingredient, 75 days before marketing the product.¹ Notice to FDA does not begin an in depth review process, however—unless FDA determines the ingredient is not a proper dietary ingredient or is unsafe, it cannot prevent a manufacturer from selling the product at issue.

The guidance FDA released in August 2016, five years after the previous draft guidance document, describes the conditions under which dietary supplement suppliers and manufacturers must submit NDI notifications, the information FDA will accept in their submissions, and the process they must follow. This guidance will play a critical role in improving industry compliance with FDA standards and clarifying a process often fraught with confusion and a lack of transparency. While I appreciate the great effort FDA has made to draft comprehensive guidance through an inclusive process, this brief comment will outline ways in which FDA can

¹ Congressional Research Service, *Regulation of Dietary Supplements* (May 6, 2013).

increase the clarity of its guidance, improve transparency in the NDI process, and protect consumers.

Clarity

One of the stated goals of the FDA in drafting this guidance has been to ensure the supplement industry understands when an NDI notification is required and how it should be submitted.² Several provisions in the guidance, however, would benefit from additional clarity.

For example, the circumstances under which manufacturers must file an NDI notification for ingredients generally recognized as safe (GRAS), are vague. Sections IV B (2) and (3) describe whether NDI notifications are necessary for GRAS ingredients and the standard that applies to GRAS ingredients that may not require an NDI notification. These sections, however, do not provide clarity on which “conventional foods” marketed outside the United States qualify for the GRAS exception and how use at a specific “intake level” – which can effect FDA’s determination of the ingredient’s safety – applies to GRAS ingredients that are exempt from notification. Similarly, these provisions do not address what impact, if any, the August 2016 GRAS rule will have on dietary supplement manufacturers.³

Additionally, there is a lack of clarity surrounding when a manufacturer can use the Masterfile of a competitor when submitting an NDI notification. While the guidance clearly permits this practice under certain circumstances, it contains little direction concerning the information manufacturers must provide to show their ingredients share similar qualities and uses with ingredients described in an existing Masterfile.⁴

Furthermore, companies initially determine whether or not they are required to file, however, the guidance does not thoroughly outline the documentation companies should retain to prove they have no obligation to submit an NDI. Without a more thorough explanation of FDA expectations regarding document retention, companies will be ill-prepared to respond to queries from FDA inspectors and other officials.

Transparency

Increasing transparency in the dietary supplement marketplace is an essential step toward enabling Americans—and their physicians—to make informed decisions about the products they consume. Additional information for consumers is even more critical given the lack of FDA pre-market approval or safety and efficacy testing for supplements. Today, most FDA enforcement authority arises after a manufacturer introduces a product to the market, which has allowed numerous adulterated and fraudulent products to reach consumers. During the past several years, for example, products containing ingredients like DMAA, oxilofrine, and picamilon—

²*Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues*, (August 2016) Section I.

³ <https://www.federalregister.gov/documents/2016/08/17/2016-19164/substances-generally-recognized-as-safe>

⁴ *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues*, (August 2016) Section IV (C)(4).

ingredients that should not have received an acknowledgment in the NDI notification process—have appeared online and at U.S. retailers.⁵

Despite these dangers, consumers examining the labels on dietary supplement packaging have no way of knowing whether manufacturers submitted NDIs for the products contained within. Yet while FDA has the authority to educate the public through releasing a list of submitted NDI notifications—and in fact published a similar list of products submitted between 1995 and 2001⁶—the proposed draft guidance does not provide for a public listing of notifications. I urge FDA to modify its draft guidance to include a provision for the publication of a list of all submitted NDI notifications, including the name of the ingredient, the name of the submitting firm, FDA’s response to the NDI notification, and a link to the notification on the Federal Register.

In addition to a list of NDI notifications, consumers should also have access to any submitted safety information FDA has deemed non-proprietary, as well as any assessments FDA has made in response, to inform their decision making. Currently, all NDI notifications appear in the Federal Register 90 days after submission, but finding these notifications is a time-consuming and cumbersome process. By making these records more readily accessible, FDA could increase public awareness of the NDI notification process and promote proper compliance with its guidance.

Finally, section IV(A)(4)(b)(11) of the proposed draft guidance states that FDA will consider creating a list of grandfathered ingredients, which have existed on the market since before October 15, 1994, are not considered NDIs, and consequently do not require a notification to FDA. While I support the creation of such a list to increase consumer awareness, FDA should also make public any information forming the basis for the list, as well as specify the form in which grandfathered ingredients appeared prior to 1994.

Encouragement and Enforcement

Although the dietary supplement market has grown from 4,000 products in 1994 to well over 55,000 products today, manufacturers have submitted fewer than 800 NDI notifications during this period.⁷ From 1994 to 2004, FDA sent no warning letters and took no enforcement actions against manufacturers for failing to submit an NDI,⁸ and between 2012 and June of 2015 they conducted fewer than 60 enforcement actions, including warning letters.⁹ While FDA

⁵ *FDA Sends Five warning Letters Over Supplements Containing Picamilon*, Nutraingredients-USA.com, (December 2015) (online at: <http://www.nutraingredients-usa.com/Regulation/FDA-sends-five-warning-letters-over-supplements-containing-picamilon>); *Banned workout stimulant found in 14 dietary supplements*, Military Times, (April 2016) (online at: <http://www.militarytimes.com/story/military/2016/04/07/banned-workout-stimulant-found-14-dietary-supplements/82751200/>).

⁶ *New Dietary Ingredients in Dietary Supplements - Background for Industry*, U.S. Food and Drug Administration (online at: <http://www.fda.gov/Food/DietarySupplements/ucm109764.htm>) (Accessed September 29, 2016).

⁷ *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues*, (August 2016) Section III.

⁸ *Is DMAA forcing FDA's hand on NDIs?*, Nutrition Business Journal, (May 2012)(online at: <http://www.newhope.com/supplements/dmaa-forcing-fdas-hand-ndis>).

⁹ Documents provided by FDA (August 18, 2015).

intends its draft guidance to increase the rate of manufacturer compliance with the NDI notification process,¹⁰ there is almost nothing in the guidance that outlines the consequences for non-compliance. For this guidance to achieve its desired effect on industry behavior, FDA must make clear it will respond to any failure by manufacturers to submit required NDI notifications with strong enforcement action.

As currently written, the draft guidance includes little discussion of FDA enforcement authority. This is particularly alarming given that FDA has the sole authority to bring enforcement actions against companies for failure to file an NDI notification. And simply explaining to manufacturers that FDA will investigate a failure to notify based on “factors relating to public health, such as potential for risk, extent of public exposure to the ingredient, and association with adverse events,”¹¹ will not provide a strong deterrent against non-compliance. FDA must make clear to manufacturers that *any* failure to comply with the notification requirements of DSHEA will be investigated and appropriate enforcement actions will be taken.

By no means can the draft NDI guidance provide a complete fix for every problem in the dietary supplement industry or the many loopholes in DSHEA. FDA has, however, taken a much needed step toward creating a safer and more transparent industry. Given the ongoing public safety concerns involved, I urge the FDA to quickly consider this comment and others and finalize its guidance as soon as is possible. American consumers cannot afford to wait for another five years.

Sincerely,



Senator Claire McCaskill

¹⁰ *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues*, (August 2016) Section III.

¹¹ *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues*, (August 2016) Section IV (A)(b)(11).