NDI Notifications Are Not Swept Aside As New Drugs - FDA

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Suggesting the investigational new drug route for a combination of a dried root ingredient and a synthetic light metal derivative is not a sign FDA is sending all new dietary ingredient notifications down the pharmaceutical track.

Daniel Fabricant, director of FDA's Division of Dietary Supplement Programs, said the agency's recent response to **PharmaRoth Labs. Inc.**'s March 2013 NDI for its nutraceutical *Sucanon* was based on the claim made for the ingredient and its pharmacological profile.

"I don't see how this is a dietary ingredient," Fabricant said, adding, "If it's not a dietary ingredient, the only option is for it is to be a drug."

Las Vegas-based PharmaRoth says its product is an insulin sensitizer that helps treat type 2 diabetes, lowering blood sugar by increasing muscle fat and the liver's sensitivity to insulin. Sucanon contains a natural ingredient derived from a dried tricosanthis plant root and a synthetic ingredient derived from a form of the light metal molybdenum *(see story p.6, "PharmaRoth Looks Abroad With Type 2 Diabetes Product After NDI Notification Decision")*.

Additional NDI information could be submitted to FDA in support of allowing the ingredient's use in dietary supplements. Should FDA later not question its safety as a supplement ingredient and should PharmaRoth not pursue the pharma application track, Sucanon potentially could become available in nutritionals marketed in the U.S.

"Speaking generally, the prohibition is on if you start out on the IND route ... then you can't just go, 'Hey, I'm going to be a dietary supplement,'" Fabricant said.

Food and drug attorneys also noted FDA is clear that an IND subject precludes an ingredient's use in supplements.

"What it comes down to is what comes first. The law is clear. If an ingredient is being looked at for dietary supplement ingredient status, you have to look at whether it was investigated as an investigational new drug before or after it was marketed as a supplement. Timing is everything," said Rick Collins, a partner at Collins, McDonald & Gann P.C. in Mineola, N.Y.

Claudia Lewis-Eng, of Venable LLC in Washington, pointed out that in addition to an ingredient currently or previously being an IND subject, claims made in an NDI notification could influence to suggest the IND route. She also noted if available in dietary supplements or food products in the U.S. before becoming the subject of drug applications, an ingredient can remain available in supplements.

"The IND route could preclude the use of a product from qualifying as a supplement if it was not first sold in the U.S. as a supplement before its use as a drug or before its investigation as a drug. Thus, there is still a chance it could be sold as a supplement," Lewis-Eng said in an email.

Although FDA's decision on the firm's NDI notification renders Sucanon products noncompliant with the agency's regulations, a website unaffiliated with PharmaRoth through March 21 continued offering sales of a product branded as Sucanon and claiming to help treat type 2 diabetes. The site includes a statement that consumers in the U.S. and Canada can buy up to three-month supplies.

FDA previously explained its position on whether the IND route is open to nutritional ingredients: advising Congress in 2010 that the agency will accept and evaluate petitions seeking regulatory permission to market a failed IND as a dietary ingredient; but in 2011 denying a firm's citizen petition asking for a regulation allowing marketing of an ingredient previously studied in an IND because the substance failed to qualify as a dietary ingredient (*"Ovos' Former IND Homotaurine Strikes Out As Dietary Ingredient" – "The Tan Sheet," Feb. 28, 2011*).

Asked whether more NDI notifications will be referred to the IND pathway, Fabricant said the content of each notification determines FDA's response. Ingredients making drug claims and with a non-dietary profile, for instance, could be IND candidates, while NDI notifications that make compliant claims but are not dietary ingredients will not be accepted and will not prompt IND suggestions.

"I think the intended use is everything, at least as far as we're concerned. Hopefully, people are considering that appropriately when they decide to position their product" as a nutritional supplement or a therapeutic product, Fabricant said.

"Understand that there are regulatory consequences with either route," he added.

Fabricant added that DDSP continues work on a revised draft guidance for NDI notifications, but he declined to estimate a timeline for publishing the document.

The initial draft published in July 2011 was withdrawn in June 2012 after complaints from across the industry, particularly about the draft's provisions on firms proving that ingredients were available in the U.S. before the Dietary Supplement Health and Education Act was passed in October 1994 and on the use of synthetic versions of botanical compounds in supplements (*"FDA Revision Of NDI Draft Guidance Starts With Grandfathered List" – "The Tan Sheet," Jun. 25, 2012*).

Fabricant noted that given the number and variety of nutritional supplement products available in the U.S., many likely containing ingredients not available pre-DSHEA, the 40 to 50 NDI notifications DDSP receives annually are much lower than the number that should be submitted.

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"Ovos' Former IND Homotaurine Strikes Out As Dietary Ingredient" – "The Tan Sheet," Feb. 28, 2011

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