



## Alliance for Natural Health USA

3525 Piedmont Road NE  
Building 6, Suite 310  
Atlanta, GA 30305

email: [office@anh-usa.org](mailto:office@anh-usa.org)  
tel: 800.230.2762  
202.803.5119  
fax: 202.315.5837  
[www.anh-usa.org](http://www.anh-usa.org)

ANH-USA is a regional office of ANH-Intl

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[anhinternational.org](http://anhinternational.org)

## Citizen Petition

March 15, 2018

On behalf of our more than 610,000 consumer members, the Alliance for Natural Health USA submits this petition under 21 C.F.R. Section 10.20 and 10.30 and under sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs revise its Investigational New Drug Applications Guidance to clarify that an investigational new drug application is not required for dietary supplements to conduct a study when there is no intent to seek drug approval for the product or the clinical investigations are being used to substantiate a legal dietary supplement claim.

### **A. Action Requested**

This petition requests that the Commissioner revise Section VI.D.1. of the Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can be Conducted Without an IND to clarify that an investigational new drug application is not required for dietary supplements to conduct a study when the sponsor or manufacturer or distributor has no intent to seek drug approval for the product or the clinical investigations are being used to substantiate a legal dietary supplement claim, e.g., structure/function claim or health claim.

Although portions of this Guidance have been stayed (see the Notice of Stay published in the Federal Register of October 30, 2015 (80 FR 66907)), the Food and Drug Administration (FDA) still maintains that the investigation of conventional foods or dietary supplements to diagnose, cure, mitigate, treat, or prevent a disease, continues to require an IND.

The Commissioner should remove the final paragraph of Section VI.D.1:

*However, if the clinical investigation is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312. For example, a clinical investigation designed to study the relationship between a dietary supplement's effect on normal structure or function in humans (e.g., guarana and maximal oxygen uptake) or to characterize the mechanism by which a dietary supplement acts to maintain*

*such structure or function (e.g., fiber and bowel regularity) would not need to be conducted under an IND. However, a clinical investigation designed to evaluate a dietary supplement's ability to prevent osteoporosis or to treat chronic diarrhea or constipation would need to be conducted under an IND.*

## **B. Statement of Grounds**

The FDA requires an IND for clinical trials to evaluate a dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease. However, supplements are not drugs and are not intended to diagnose, cure, mitigate, or prevent disease. A supplement company may need to conduct a study that investigates a supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease in order to substantiate a legal dietary supplement claim. Section 201(ff)(3)(B)(ii) of the FD&C Act (21 U.S.C. 321(ff)(3)(B)(ii)) excludes from the definition of a dietary supplement any “*article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food.*”

Requiring an IND naturally creates published studies, and turns a dietary ingredient into a drug if it has not been previously marketed as a dietary supplement or as a food. Thus, Section VI.D.1. of the IND Guidance means that complying with the law to substantiate a claim to legally market a dietary ingredient will turn it into a drug and threaten its very status as a marketable dietary ingredient.

The FDA promulgated Title 21 C.F.R. Part 312 to provide procedures and requirements governing the use of investigational new drugs as part of the drug approval process, and not as a way of regulating the clinical study of foods and dietary supplements. The agency made this purpose clear in the preamble to its final rule establishing Part 312, called the IND Rewrite:

*This action is one part of a larger effort by FDA to improve the agency's drug approval process . . . The objectives of the IND Rewrite final rule are to establish an efficient investigational drug process in order both: (a) To focus FDA's attention during the early phase of clinical research on protecting the safety of human test subjects . . . and (b) to facilitate consultation between FDA and drug sponsors . . . to help ensure that the design of major clinical trials is acceptable and will support marketing approval if the test results are favorable. These changes are also intended to encourage innovation and drug development while continuing to assure the safety of test subjects.*

It is therefore clear that at the time that FDA promulgated its IND regulations, the agency intended them to apply solely to articles being researched as therapeutic drugs for which new drug applications were contemplated.

In the IND Guidance, the FDA explains that an IND is needed if three conditions exist – one condition being that the research *involves a drug*. Drugs are defined under Part 321

as, among other things, “articles *intended for use* in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals.” Further, Part 312 says that IND’s are required for all products that are subject to section 505 of the FD&C Act, which pertains to new drugs.

Supplements are not covered under these regulations because supplements are not drugs intended to cure or mitigate disease. The Dietary Supplement Health and Education Act of 1994 excludes from the definition of dietary supplement “an article authorized for investigation as a new drug...for which substantial clinical investigations have been instituted and for which the existence of such investigation has been made public,” unless the article was marketed before the IND became effective.

If an IND is required for clinical investigations on a new dietary ingredient to substantiate a structure/function or health claim it could eliminate the ability to market the product as a dietary supplement. Furthermore, a supplement claiming to diagnose, cure, mitigate, treat, or prevent disease is, by definition, a misbranded drug. Thus, supplement research should not trigger IND regulations.

Furthermore, the FDA has historically regulated products based on intended use, which is determined by the manufacturer’s marketing representations and labeling of a product. Courts have consistently upheld this approach, which is also supported by past agency statements. The FDA should do the same in this case – consider the end use of the product rather than the intention of the clinical investigation to determine whether an IND is required. The FDA offers no rationale or legal basis for the IND Guidance’s departure from past agency practice to now focus on the intent of the clinical investigation to evaluate a product’s intended use.

For assurance that a study should not require an IND, signed affidavits can attest to a company or researcher’s intention to not market the supplement or food as a drug following a clinical trial assessing the therapeutic benefits of a supplement or food.

## **Conclusion**

Dietary supplements should not be subject to IND regulations intended for drugs that could eliminate the ability to market a product as a dietary supplement.

The FDA should clarify that, if the supplement under investigation is fully compliant with IRB procedures and not represented as a drug through marketing statements, and any claims made for the supplement are lawful dietary supplement claims, then FDA should not regulate the product as a drug by applying its Part 312 procedures.

Signed affidavits can attest to a company or researcher’s intention to not market the supplement or food as a drug following a clinical trial assessing the therapeutic benefits of a supplement or food.

## **C. Environmental Impact**

Petitioner claims a categorical exclusion under 21 C.F.R. §25.30(h).

**D. Economic Impact**

Pursuant to 21 C.F.R. §10.30(b), economic impact information will be submitted by the Petitioner upon the request of the Commissioner.

**E. Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,



Gretchen DuBeau, Esq.  
Executive and Legal Director  
Alliance for Natural Health USA

Cc: Mr. Steven Tave, Director, Office of Dietary Supplement Programs