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Determining Whether A Dietary Supplement Study Requires an Investigational New Drug (IND)

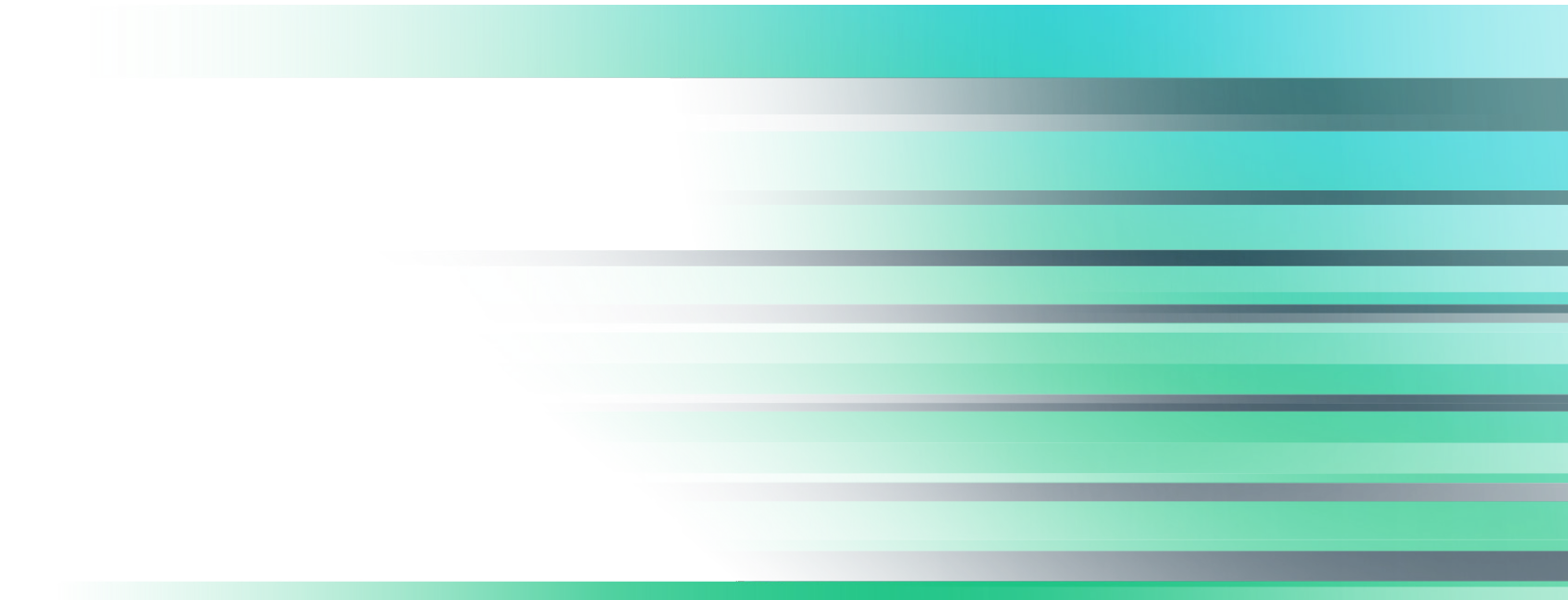
02/02/16

DESCRIPTION

Does a study that claims their dietary supplement "promotes healthy joints and cartilage" or "helps with arthritis, joint, and muscle-related aches and pains," require an IND?

TOPICS

- LEGAL REQUIREMENTS
- REGULATORY ANALYSIS



How Does An IRB Meet Its Responsibilities?

Does a study that claims their dietary supplement "promotes healthy joints and cartilage" or "helps with arthritis, joint, and muscle-related aches and pains," require an IND? How does an IRB meet its responsibilities with respect to verifying the determination of whether an IND is required for an FDA-regulated investigation?

In recent years, the IRB's role in evaluating dietary supplement studies has evolved to require an additional review step. Namely, a determination of whether an IND may be required before research is considered for approval.[1] This presents an additional burden to IRBs who may see a limited number of studies This article provides an overview of the requirements and potential actions an IRB may take in carrying out its responsibilities.

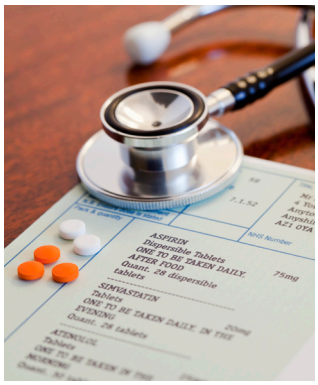
Legal requirements

Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), a dietary supplement is defined, as "a product (other than tobacco) intended to supplement the diet that bears or contains one or more dietary ingredients."[2] The dietary ingredients in these products can include vitamins, minerals, herbs and other botanicals, amino acids, other dietary substances intended to supplement the diet, and concentrates, metabolites, constituents, extracts, or combinations of the preceding types of ingredients.[3] Dietary supplements are taken by mouth and can be found in many forms such as tablets, capsules, softgels, liquids, gelcaps, or powders.[4]

Under DSHEA, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use for which it is marketed is only to affect the structure or any function of the body and not intended to be used for a therapeutic purpose.[5] Therefore, whether an IND is needed for a clinical investigation evaluating a dietary supplement is determined by the intent of the clinical investigation. If the clinical investigation is intended only to evaluate the dietary supplement's effect on the structure or function of the body, an IND is not required.[6]

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.[7]

Regulatory analysis



Evaluating "intent" begins with a determination of the "intended use" of the clinical investigation.

INTENDED USE

The intended use of a product will determine whether it is regulated as a food, dietary supplement, or a drug. FDA will consider the claims made on product's label and in its labeling and advertising as well as the end points evaluated in a clinical study when determining intended use. If a claim is made about the impact of a nutritional product on the diagnosis, cure, mitigation, treatment, or prevention of a disease or health related condition, the product will be regulated as a drug. If a study evaluates a drug or disease end point or indication, the substance being studied will be deemed a drug and FDA likely will require an IND.

Recent FDA warning letters have presented a number of examples of claims that the FDA has determined are drug claims, including:

- "Promotes healthy joints & cartilage"[8]
- "Super Arthgold may improve the blood circulation, which can help relieve soreness caused by lactic acid build-up in the muscle tissues. Better blood flow can also contribute to increased range of motion in the joints, which may help arthritis and joint pain."[9]
- "Each capsule of DigestaCure® contains 500mg of pure, concentrated immune modulating components, for the restoration of immunity and elimination of autoimmunity."[10]
- "Helps stop sore throat on contact"[11]
- "Helps get rid…of inflammation"[12]
- "Wound healing…Pain Relief & Burn Therapy…"[13]

FDA does not consider the purpose of a study to be therapeutic if the study simply measures the effect of a nutritional product on the structure or function of the body or examines the mechanism by which the product exerts its effect.

Examples given in the FDA guidance include:

- An IND would not be required for 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.

DRUG OR DISEASE PURPOSE VS. STRUCTURE/FUNCTION

IRBs must carefully assess whether a research study's purpose is evaluating a drug or disease indication or end point, versus the effect of the nutritional product on the structure or function of the body. To determine whether a study has a drug or disease purpose, we refer to the definition of "disease" promulgated in the FDA regulations for dietary supplements. "Disease" is defined as damage to an organ, part, structure, or system of the body such that the organ, part, structure, or system does not function properly (e.g., cardiovascular disease) or a state of health leading to such dysfunction (e.g., hypertension).[14]

> "The intended use of a product will determine whether it is regulated as a food, dietary supplement, or a drug."

FDA has further defined "disease claims" as including any statement that a product:

- Has an effect on a specific disease or class of diseases;
- Has an effect on the characteristic signs or symptoms of a specific disease or classic diseases;
- Has an effect on an abnormal condition associated with a natural state or process, if the abnormal condition is uncommon or can cause significant or permanent harm;
- Belongs to a class of products that is intended to diagnose, mitigate, treat, cure, or prevent a disease or class of diseases;
- Is a substitute for a product that is a therapy for a disease;
- Augments a particular therapy or drug action that is intended to diagnose, mitigate, treat, cure, or prevent a disease or class of diseases;
- Has a role in the body's response to a disease or to a vector of a disease; Treats, prevents, or mitigates adverse events associated with a therapy for a disease, if the adverse events constitute diseases; or
- Otherwise suggests an effect on a disease or diseases.[15]

ROLE OF THE SPONSOR, IRB, AND FDA

Sponsors would be well served to include an explanatory letter with the initial submission of any study involving a dietary supplement. Such explanation can include a copy of any available supporting documentation (e.g., letter from the sponsor or FDA with rationale supporting the determination, information about prior studies conducted with this dietary supplement). During initial review of the study, the IRB will review the protocol and any submitted explanation to determine if an IND may be required to conduct the study.

When an IRB determines that an IND is or may be required, the following options are usually sought:

1. Requesting a formal response from the FDA that an IND is not required; or,
2. Requiring submission of an IND to the FDA (where the FDA may use its enforcement discretion and determine the IND is not required) and delay of approval until the IND is in effect in accordance with 21 CFR 312.40.

These options are in line with FDA guidance, which urges IRBs to follow their written procedures for resolving controverted issues and delaying approval until the matter is resolved.

Conclusion

If an IRB questions whether an IND may be required, the IRB should not approve the study until the IND issue is resolved. In reviewing such studies and determining intended use, IRBs rely on Board members with expertise in reviewing alternative and complementary medicine studies; for example, dietary supplements, cosmetic products, and herbal products. However, IRBs that lack such expertise should bolster their board with a member or consultant who can weigh in on the protocol and IND determination.

REFERENCES

1. Guidance for IRBs, Clinical Investigators, and Sponsors – IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed, August 2013 (Final Guidance).
2. 21 U.S.C. 321(ff)
3. Id.
4. 21 U.S.C. 350(c)(1)(B)
5. Guidance for Clinical Investigators, Sponsors, and IRBs – Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND, September 2013 (Final Guidance).
6. Id.
7. Id.
8. FDA Warning Letter to Health Science Foundation, dated 08/18/14.
9. Id.
10. FDA Warning Letter to Pristine Nutraceuticals, LLC, dated 01/21/15.
11. FDA Warning Letter to Aloe Man, Inc., dated 01/08/15.
12. Id.
13. FDA Warning Letter to PI Pharma Inc., dated 10/31/14.
14. 21 C.F.R. § 101.93(g)
15. Id.

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