Probiotics and Clinical Research

Modified: November 2019

Background:

Researchers from a diverse array of scientific disciplines have focused on opportunities and areas for responsible clinical research involving the possible beneficial health effects of “probiotics.” Investigators and researchers should be aware that not all clinical research involving probiotics reasonably falls within the requirements of the “investigational new drug” (IND) rubric administered and enforced by the US Food and Drug Administration.

1. **Q: Do research studies involving probiotics require an Investigational New Drug (IND) application?**

   Maybe. The IND rubric does not apply to all possible types of clinical research. As a general rule, the IND rubric only applies when the “intended use” of a product or substance serves to categorize the test substance as a “new drug” or “biological product.” “Intended use” is primarily determined by the sponsor’s intent which can be manifested in product labeling and claims as well as in the terms and endpoints of the test protocol.

   It follows that clinical investigations of products or substances regulated as “foods” and “dietary supplements” are not subject to the rigors of the IND process unless the intended use or endpoint(s) investigated serve to also categorize the substance as a “drug” and “new drug” or “biological product.”

2. **Q: What type of research does require an IND?**

   Research that involves a new “drug” or “biologic.” An article is a “drug” if it is intended for the cure, mitigation, treatment, diagnosis, or prevention of disease.

   Determining whether a product is a “biological product” can be more complex. An article is a “biological product” if it contains a “virus, therapeutic serum, toxin, anti-toxin, vaccine, blood, blood component or derivative, allergenic product, or protein (except any chemically synthesized polypeptide) or analogous product…applicable to the prevention, treatment, or cure of a disease condition.”

3. **Q: How is the differentiation made as to whether the IRB will require the investigator to obtain an IND?**

   First, the FDA has no guidance which makes clear when research with a probiotic will require an IND. Thus, decisions by the IRB may change over time, and will be directed by the intent of the research.

   As a general rule, when a clinical investigation focuses on an endpoint involving the cure, mitigation, prevention, treatment, or diagnosis of disease, the IND rubric comes into play. On the other hand, if the focus of the study is on the effect of a substance solely on the structure or function of the human body and no disease endpoint is implied or on an endpoint falling within the scope of a “health claim” or “medical food,” the IND requirements should not, as a general rule come into play.

   FDA has, however, issued detailed regulations that differentiate between structure or function claims appropriate for dietary supplements (and by inference, appropriate for foods) and “drug” claims that...
may not be made on behalf of a dietary supplement or on behalf of a food without prior FDA authorization. For example, FDA has recognized that a claim that a probiotic food or supplement “helps maintain flora” is an appropriate structure/function claim because it does not imply an effect on disease and because it does not reference a drug, drug action, or therapy and thus would not require an IND. That said, the agency has also stated that a claim that a probiotic product “helps individuals using antibiotics to maintain normal intestinal flora” is an implied drug claim to the effect that using such a product mitigates a disease condition and thus would require an IND.

4. When and how do you verify an IND is or is not required?

The IRB may be unsure if an IND is required, and will ask the investigator to submit a request to the FDA for them to make that determination. Please refer to the Investigator Guideline on “Research Using FDA Test Articles” for guidance on this process.

5. What are examples of the differences between Structure/Function and Drug Claims?

<table>
<thead>
<tr>
<th>Structure/Function Claim</th>
<th>Drug Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>(no prior approval needed – no IND)</td>
<td>(approval needed – need IND)</td>
</tr>
<tr>
<td>• Helps maintain normal cholesterol levels</td>
<td>• Lowers cholesterol</td>
</tr>
<tr>
<td>• Maintains healthy lung function</td>
<td>• Maintains healthy lung function in smokers</td>
</tr>
<tr>
<td>• Provides relief of occasional constipation</td>
<td>• Provides relief of chronic constipation</td>
</tr>
<tr>
<td>• Suppresses appetite to aid weight loss</td>
<td>• Suppresses appetite to treat obesity</td>
</tr>
<tr>
<td>• Supports the immune system</td>
<td>• Supports the body’s antiviral capabilities</td>
</tr>
</tbody>
</table>

References:

Degnan, Fred. Clinical studies involving probiotics When FDA’s investigational new drug rubric applies—and when it may not Gut Microbes 3:6, 485-489; November/December 2012; © 2012 Landes Bioscience