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ALERT

FDA Proposes New Exemptions From IND Regulations for Certain Drug Use Clinical Studies of Food, Dietary Supplements, and Cosmetic Products

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In what could be a game-changer to the dietary supplement and food industry, the U.S. Food and Drug Administration (FDA or Agency) is proposing to amend the investigational new drug (IND) regulations to exempt clinical studies of foods for human consumption (including dietary supplements) and cosmetic products that are being investigated for drug uses, assuming the studies meet certain criteria. The IND regulations currently exempt certain drug studies on drug products that are legally marketed, assuming the studies do not significantly increase the risk of the product through a change in the dose level or route of administration, or a shift in patient populations, for example. The proposed rule would expand these exemptions to include food and cosmetic products.

FDA is proposing to have two pathways for obtaining an exemption: a self-determined exemption and an FDA-determined exemption. Under the self-determination pathway, a Sponsor of a drug use study of a conventional food for human consumption, a dietary supplement, or a cosmetic can determine the study is exempt from the IND regulations (including an exemption from requesting FDA specifically exempt the study) if it meets the following criteria:

- The study will not be used to support a future IND, a drug development plan, or a labeling change that would render the product an unlawfully marketed drug (*i.e.*, marketing a dietary supplement to treat a disease);

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- The study is conducted consistent with requirements for institutional review board (IRB) review and informed consent (21 CFR Part 50 and Part 56);
- The study complies with the existing regulations for promotion and commercial distribution of investigational drugs (21 CFR 312.7);
- There is no change to the route of administration of the product from its current lawful use;
- The study meets other criteria to protect human subjects' safety and welfare (including, but not limited to, a requirement that no subjects are less than 12 months old, exclusion of immunocompromised subjects or those with a serious or life-threatening disease, exclusion of pregnant and lactating subjects, no study procedures beyond those normally encountered, product used within its normal conditions of use).

The second pathway is an FDA-determined exemption from the IND regulations. This can take two forms. First, a Sponsor can submit the request to FDA, and this option would be appropriate for those studies that meet the criteria above for self-determination, except there may be questions of health, safety, and welfare that the Sponsor does not think will introduce a significant risk to subjects. The Sponsor would include a description of the study and a justification that the study does not pose such a risk to subjects for FDA review, who would then grant an exemption if they agree that the study does not pose a significant risk to the health and safety of the subjects, or as FDA states "decrease the acceptability of the risks" to the subjects. The second form is an FDA-initiated exemption, which may occur when an IND has been submitted to the FDA, but review of the application reveals that the study meets the criteria for an FDA-determined exemption. The Agency indicates that in this case, they would refuse to accept the IND. FDA also provides an important caveat that, if the Agency becomes aware of any information that suggests there is an unacceptable risk to the health, safety, and welfare of the subjects or that it no longer meets the criteria for exemption, either self-determination or the FDA-determined exemption can be revoked.

What Is Not Exempt

In what will no doubt be a significant disappointment to the food and cosmetic industry, the new exemption process would not exempt studies that are intended to support a drug claim on a conventional food or cosmetic, or a study of a dietary supplement for treatment of disease, and studies that would support a labeling claim on a food or cosmetic package are similarly not exempt. In the proposed rule, FDA discusses the types of studies it envisions falling under this exemption as those conducted by researchers or physicians independent of manufacturers to understand the impact of a food or cosmetic on a disease or condition, without the desire to market a product. But these studies also benefit industry, and could ultimately act as proof of concept research that justifies further research under an IND for potential claims. This is a unique opportunity for new studies to be conducted that could provide valuable insight on the use of conventional foods and cosmetics as potential treatments for diseases.

Potential Issues: Timing and the Use of the Refuse to Accept Action

One aspect of the FDA-determined submission that is notably absent is the review period. FDA describes the process for the submission of a request for determination, but fails to provide any review clocks or estimates. This is problematic for industry or any Sponsor, who need to plan for study resources and schedules. It is likely that public comments will reflect this omission, and FDA will hopefully address this in the final rule.

Another potential issue is that FDA intends to "refuse to accept" the IND that is filed and determined to be exempt. While we understand that this is the process currently used, albeit on a case-by-case basis, this language could prove problematic with this new proposed pathway without further clarification of a refuse to file status or perhaps a new application outcome category. A refusal to accept is often viewed as a negative outcome, suggesting a deficient or unsafe application, and could have serious implications for small businesses and those seeking funding for products. If the company is publicly traded, such a refusal would be disclosed, and further explanation would be needed during due diligence activities and investor conversations. It would be more transparent and accurate for FDA to apply a new determination, such as labeling the submission "Exempt from IND Regulations" or some other term of art, instead of relying on the refusal language, which could be seen as detrimental.

The proposed exemption from IND regulation for certain clinical studies of foods for human consumption (including dietary supplements) and cosmetic products could be extremely valuable to the food and cosmetic industry, and promote new research into drug uses for these products that were previously unavailable without the heavy regulatory burden of an IND. FDA is seeking comments to the rule until March 9, 2023, and we will closely monitor the comments and the language in the final rule when released to assess any changes from the current proposal. If you or your company need assistance in submitting comments or have questions regarding the analysis, the Food & Drug team at Wiley is available for assistance.