December 9, 2014

IMPORTANT DRUG WARNING REGARDING USE OF DIETARY SUPPLEMENTS IN IMMUNOCOMPROMISED PERSONS

Subject:	**Risk of Invasive Fungal Disease in Immunocompromised Persons Given Dietary Supplements Formulated to Contain Live Bacteria or Yeast**

Dear Healthcare Provider:

The purpose of this letter is to inform you of important safety information regarding use of dietary supplements containing live bacteria or yeast in immunocompromised persons.

Risk of Invasive Fungal Disease with Use of a Dietary Supplement in Immunocompromised Persons

- A premature infant administered a dietary supplement, ABC Dophilus® Powder (Solgar®), as part of in-hospital course of treatment, developed gastrointestinal mucormycosis caused by the mold *Rhizopus oryzae* and died.
- *Rhizopus oryzae* mold was found to be present as a contaminant in an unopened container of the ABC Dophilus Powder, which is formulated to contain three species of live bacteria.
- Gastrointestinal mucormycosis primarily occurs in immunocompromised persons, such as prematurely born infants.

The U.S. Food and Drug Administration (FDA) along with the Centers for Disease Control and Prevention (CDC) and the Connecticut Department of Public Health are investigating the death of this preterm infant who developed gastrointestinal mucormycosis.[1] In mid-November, Solgar issued a recall for certain lots of ABC Dophiilus Powder and public health warnings were issued advising customers and consumers not to use the recalled product.

Information on Safety and Manufacturing and Testing Standards

In light of the case of fatal gastrointestinal mucormycosis described above, FDA is informing healthcare providers that dietary supplements, including those that are formulated to contain live bacteria or yeast, are generally not regulated as drugs by the FDA. As such, these products are not subject to FDA's premarket review or approval requirements for safety and effectiveness, nor to the agency's rigorous manufacturing and testing standards for drugs, including testing for extraneous organisms. However, FDA is aware that some products marketed as dietary supplements are used by providers in the practice of medicine as drugs (e.g., to treat, mitigate, cure, or prevent a disease or condition) and is providing the following clarification for provider use.

[1] For additional information on the investigation see the following links:
http://www.fda.gov/Food/RecallsOutbreaksEmergencies/Outbreaks/ucm423830.htm
http://www.cdc.gov/fungal/rhizopus-investigation.html

Prescriber Action

In considering the use of any dietary supplement containing live bacteria or yeast in immunocompromised persons, health care providers should note that these products are not subject to FDA's premarket review and approval requirements for safety and effectiveness or to the manufacturing and testing standards for products regulated as drugs by FDA.

FDA is aware of recommendations in the peer reviewed literature regarding the use of live bacteria in the prevention of necrotizing enterocolitis in premature infants.[2] However, FDA cautions that a systematic review of the clinical trial literature found inadequate documentation of the safety of the interventions[3], and advises practitioners to approach the application of these interventions with caution.

FDA encourages health care providers who use dietary supplements containing live bacteria or yeast as drugs (e.g., to treat, mitigate, cure, or prevent a disease or condition) to submit an Investigational New Drug Application (IND) for FDA review.[4] FDA's primary goals in reviewing an IND are to ensure the safety and rights of subjects and to help ensure that the quality of the scientific study of drugs is adequate to permit an evaluation of the drug's effectiveness and safety. Therefore, part of the FDA's review of an IND includes assessment of the quality of manufacturing and testing.

Reporting Adverse Events

Health care providers and consumers are encouraged to report adverse events following use of dietary supplements both to the manufacturer using the address or phone number which is required to be on the product label and to the FDA. Visit www.safetyreporting.hhs.gov to submit a report online, or call 1-800-FDA-1088.

Sincerely,

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[2] http://www.ncbi.nlm.nih.gov/pubmed/25236307
[3] http://www.ahrq.gov/research/findings/evidence-based-reports/probiotsum.html
[4] General principles of the IND submission, 21 CFR 312.22(a):
http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/default.htm