

WARNING REGARDING USE OF PROBIOTICS IN PRETERM INFANTS

Subject: Risk of Invasive Disease in Preterm Infants Given Probiotics Formulated to Contain Live Bacteria or Yeast

September 29, 2023

Dear Healthcare Provider:

The U.S. Food and Drug Administration (FDA) is providing important safety information to healthcare providers on the use of products containing live bacteria or yeast (commonly called probiotics) in preterm infants in hospital settings.

Risk of Invasive Disease with the Use of Probiotics in Preterm Infants

- The FDA is warning that preterm infants who are given probiotics are at risk of invasive, potentially fatal disease caused by the bacteria or fungi contained in probiotics.
- A preterm infant, birthweight <1000 g, who was administered a probiotic, Evivo with MCT Oil (Infant Health), as part of in-hospital care, developed sepsis caused by the bacterium *Bifidobacterium longum* and subsequently died.
- Evivo with MCT Oil is a probiotic formulated to contain the live bacterium, *Bifidobacterium longum* subsp. *infantis*.
- The FDA is investigating the death of this preterm infant. Genomic sequencing data demonstrate the bacterium that caused sepsis in this infant was a genetic match to the bacteria contained in this probiotic.

Information on Probiotic Safety

The FDA cautions that microorganisms contained in probiotics have been reported in the medical literature as causing bacteremia or fungemia, sometimes with a severe clinical course, in very preterm or very low birthweight (VLBW) infants.¹⁻⁴

Moreover, the American Academy of Pediatrics states “Given the lack of FDA-regulated pharmaceutical-grade products in the United States, conflicting data on safety and efficacy, and potential for harm in a highly vulnerable population, current evidence does not support the routine, universal administration of probiotics to preterm infants, particularly those with a birth weight of <1000 g.”⁵

The FDA is also reminding healthcare providers that FDA has not approved any probiotic product for use as a drug or biological product in infants. The FDA is aware that some unapproved, unlicensed probiotics are nonetheless sold for use to treat or prevent a disease or condition in infants, including to reduce the

risk of necrotizing enterocolitis (NEC) in preterm infants. Healthcare providers should be aware that these products have not undergone the FDA's rigorous premarket review evaluation for safety and effectiveness, nor have they been evaluated for compliance with the agency's rigorous manufacturing and testing standards for drugs and biological products, including testing for extraneous organisms.

The FDA reminds healthcare providers who administer probiotics containing live bacteria or yeast to treat, mitigate, cure, or prevent a disease or condition that they are required to submit an [Investigational New Drug Application \(IND\)](#) to the agency.

Reporting Adverse Events

The FDA encourages healthcare providers and consumers to report adverse events following use of probiotics both to the manufacturer using the address or phone number which is required to be on the product label and to the FDA. Visit <http://www.fda.gov/MedWatch/report.htm> to submit a report online or call 1- 800-FDA-1088.

Sincerely,

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¹⁻⁴ Case reports of bacteremia and fungemia from probiotic use in preterm infants:
<https://pubmed.ncbi.nlm.nih.gov/27532215/>, <https://pubmed.ncbi.nlm.nih.gov/25472946/>,
<https://pubmed.ncbi.nlm.nih.gov/28133894/>, <https://pubmed.ncbi.nlm.nih.gov/32859326/>

⁵ Poindexter B. Use of probiotics in preterm infants. *Pediatrics* 2021;147(6):June 2021:e2021051485.
<https://publications.aap.org/pediatrics/article/147/6/e2021051485/180282/Use-of-Probiotics-in-Preterm-Infants>