

Statement on FDA Warning of Probiotics in Preterm Infants



October 6, 2023

The Necrotizing Enterocolitis (NEC) Society is a 501(c)(3) organization dedicated to advancing NEC research, education, and advocacy. Our organization is led by patient-families and clinician-researchers who intimately understand the devastation of losing a child or patient to NEC. We work tirelessly to help accelerate improved prevention and treatment strategies for infants at risk of this cruel disease.

The NEC Society does not advocate for or against the prophylactic use of probiotics in the NICU. The NEC Society *does* urge the neonatal community to openly communicate and partner with families to collaboratively evaluate the evidence, risks, and benefits of various treatments, including probiotics, for their unit's unique patient population. We highlight the risks and benefits of probiotics in our [Statement on Probiotics](#) and [Neonatal Probiotics Toolkit](#).

Pursuing safety for our most vulnerable patient population is essential. As the only organization representing families affected by NEC in the United States, it is vital for the FDA and the broader neonatal community to acknowledge the overwhelming burden of NEC. NEC is a life-altering diagnosis and the single most common cause of death in extremely preterm infants between two weeks and two months of age. Accordingly, it is imperative for the NEC Society to respond to the FDA's warning of probiotic use in preterm infants. As such, the NEC Society contends:

- The death of a child is tragic and devastating. The NEC Society works tirelessly to help prevent necrotizing enterocolitis because 8,951 babies died from NEC between 1999-2020 and currently approximately 500 infants die from NEC every year in the United States¹. The NEC Society knows the grief of watching our children and patients struggle, suffer, and die from NEC. For infants who survive the disease, we know that NEC does not end when families leave the NICU. Survivors often endure severe lifelong digestive and neurological complications throughout childhood and into adulthood²⁻⁴.
- In clinical studies, probiotic supplementation has been shown to reduce the risk of NEC, late-onset sepsis, and mortality in preterm infants.⁵⁻⁷ It is one tool with the potential to help prevent this deadly disease. As with many other widely used treatments in the NICU, probiotics have both risks and benefits. One rare risk is infection from the probiotic itself, as highlighted in the alert from the [FDA](#). It is important to emphasize that the potential for death from probiotics is exceedingly [rare](#), whereas death and severe morbidity from NEC is stubbornly high.
- A multi-disciplinary team, including patient-families, should evaluate safety risks, in addition to the literature-supported benefits and the unique characteristics of each NICU. We highlight the

benefits and risks of probiotic supplementation in our [Probiotic Toolkit](#).

- Given the paucity of pathways to bring about promising medications and treatments for vulnerable neonates, it is the physicians who should decide how legally available treatments or tools, such as dietary supplements, drugs, devices, and other therapies, are used and tailored in their practice of medicine with their complex patients in the NICU, considering the best available evidence and in partnership with families.
- The NEC Society urges the neonatal community not to waiver in our shared goal of preventing NEC and improving outcomes for all infants in the NICU.
- We are working tirelessly to advance research and optimize care practices to improve outcomes. More research and ongoing evaluation are imperative to the protection of infants in the NICU.
- We reaffirm our [Statement on Probiotics](#).
- **The NEC Society is eager to engage with the FDA to represent our patient-families and clinician-researchers. The NEC Society is uniquely positioned to help ensure the neonatal community, from families to clinicians and scientists, can optimize the strategies and tools available to best support the health of infants and protect them from the devastating risks of necrotizing enterocolitis.**

1. Wolf MF, Rose AT, Goel R, Canvasser J, Stoll BJ, Patel RM. Trends and Racial and Geographic Differences in Infant Mortality in the United States Due to Necrotizing Enterocolitis, 1999 to 2020. *JAMA Netw Open*. 2023;6(3):e231511. doi:[10.1001/jamanetworkopen.2023.1511](https://doi.org/10.1001/jamanetworkopen.2023.1511)

2. Canvasser J, Patel RM, Pryor E, et al. Long-term outcomes and life-impacts of necrotizing enterocolitis: A survey of survivors and parents. *Semin Perinatol*. 2023;47(1):151696. doi:[10.1016/j.semperi.2022.151696](https://doi.org/10.1016/j.semperi.2022.151696)

3. Federici S, De Biagi L. Long Term Outcome of Infants with NEC. *Curr Pediatr Rev*. 2019;15(2):111-114. doi:[10.2174/1573396315666181130144925](https://doi.org/10.2174/1573396315666181130144925)

4. Pike K, Brocklehurst P, Jones D, et al. Outcomes at 7 years for babies who developed neonatal necrotising enterocolitis: the ORACLE Children Study. *Arch Dis Child Fetal Neonatal Ed*. 2012;97(5):F318-322. doi:[10.1136/fetalneonatal-2011-300244](https://doi.org/10.1136/fetalneonatal-2011-300244)

5.Gray KD, Messina JA, Cortina C, et al. Probiotic Use and Safety in the Neonatal Intensive Care Unit: A Matched Cohort Study. *J Pediatr*. 2020;222:59-64.e1. doi:[10.1016/j.jpeds.2020.03.051](https://doi.org/10.1016/j.jpeds.2020.03.051)

6.Agha L, Staiger D, Brown C, Soll RF, Horbar JD, Edwards EM. Association of Hospital Adoption of Probiotics With Outcomes Among Neonates With Very Low Birth Weight. *JAMA Health Forum*. 2023;4(5):e230960. doi:[10.1001/jamahealthforum.2023.0960](https://doi.org/10.1001/jamahealthforum.2023.0960)

7. Wang Y, Florez ID, Morgan RL, et al. Probiotics, Prebiotics, Lactoferrin, and Combination Products for Prevention of Mortality and Morbidity in Preterm Infants: A Systematic Review and Network Meta-Analysis. *JAMA Pediatrics*. Published online October 2, 2023. doi:[10.1001/jamapediatrics.2023.3849](https://doi.org/10.1001/jamapediatrics.2023.3849)