When It Comes To Reading Infant Probiotic Labels, What's Most Important?

Rebbeca M Duar, PhD

When it comes to choosing a probiotic for your infant patients, product quality and label transparency should be top priorities. A concise and coherent label is an essential component of a product's package, as it enables clinicians to easily differentiate and critically evaluate probiotic products through an evidence-based approach. However, according to a recent study, over 60% of probiotic supplements sold in the US are missing key components in their labels.[1] This guide is aimed to help health professionals analyze, understand and interpret probiotic product labels to make informed decisions when selecting high-quality, fit-for-purpose, probiotics for their infant patients. The principles outlined are similar to those recommended for evaluating dietary supplements and food products.

1. Ensure proper identification of the probiotic bacteria

Having the proper nomenclature is crucial to conduct an evidence-based selection of a probiotic product. Where this information is located can vary. In some it is located in the ingredients list, while others have a separate list of bacterial strains. The placement is not as important as having the right information. The genus, species, subspecies (when applicable) and importantly, the strain names must be clearly listed. For example, in the probiotic strain *Bifidobacterium longum* subspecies *infantis* EVC001, *Bifidobacterium* is the genus, *longum* the species, *infantis* the subspecies and EVC001 is the strain name. When conducting research on the evidence for a particular product, use the strain name to connect the product with peer-reviewed data. Keep in mind, each strain is genetically unique and the benefits of one strain may be very different from others. Similarly, safety and efficacy associated with specific strains should not be generalized to other probiotic products.[2] For instance, a recent study found important genetic differences among *B. infantis* strains added to infant probiotic products.[3] These differences were found to be related to the wide variation in the ability of strains to utilize human milk oligosaccharides (HMOs). H5-positive strains were found to be fully functional and able to efficiently metabolize HMOs. On the other hand, H5-negative strains were found to have critical genetic mutations that negatively affect their ability to access HMOs and colonize the infant gut. These findings are relevant as the benefits observed when infants are colonized with *B. infantis* EVC001, an H5-positive strain, are strongly associated with the conversion of HMOs into beneficial metabolites that positively alter the biochemistry of the infant gut.[4] These biochemical changes are associated with the displacement of potential pathogens and a significant reduction in enteric inflammation.[5,4] Due to the reduced capacity to access HMOs and colonize the infant gut, it is unlikely that H5-negative strains can provide these benefits. This same study found that over 50% of products of did not list the strain name in their labels, making it impossible for health care professionals and consumers to assess the probiotic in an evidence-based manner.[3] Thus, it is advisable to steer away from products that do not list the strain and always confirm the scientific literature is aligned with the benefits claimed for a particular strain in a probiotic product.

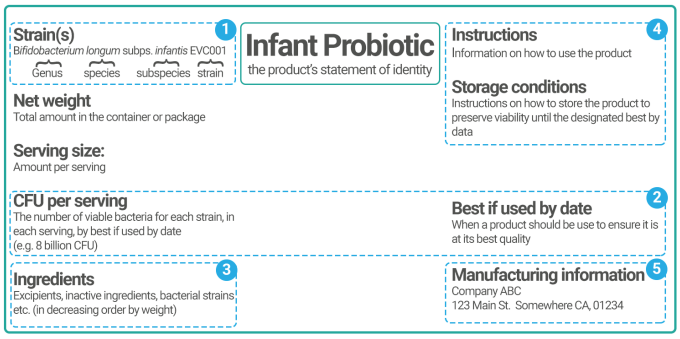
More isn't always better when it comes to probiotics

More species or strains in a probiotic product does not guarantee better health benefits. There is currently no scientific evidence demonstrating synergism between two or more strains in providing additional benefits. In fact, some common probiotic species are known to have antagonistic effects on one another.[6] Moreover, combining strains that have been studied individually does not guarantee an additive effect, which could explain why a higher number of species or strains listed on a label is associated with less peer-reviewed evidence.[1] In a recent position paper, experts from the globally recognized European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) stated that "use of a single strain with proven effectiveness is likely to be more efficacious than use of a combination of strains without proven effectiveness",[7] reiterating the notion that when it comes to probiotics, using clinically studied, well-documented strains allows for a more targeted and evidence-based approach to infant gut health.

Be wary of sudden name changes and reclassifications

Label changes and reclassifications to bacterial names and strain designations can be deceptive and and appear as as a footnote, rather than in the main label. Sudden name changes usually indicate a strain or species was misidentified or replaced, a problem that has been notorious in products containing bifidobacteria due to the technical difficulties in differentiating the species.[8] The consequences are not minor. If misidentified, comparisons of outcomes across cohorts, units or clinical trials become meaningless. If replaced, an unintended bacterial strain may be incorporated into a standard of care and which may impact patient outcomes for patients in your care. Official name changes in bacteria require agreement from a panel of international experts and when the changes take place the results are published in official journals. One example is the recent reclassification of the genus *Lactobacillus*, which was a

Rebbeca Duar is a Principal Scientist and Senior Manager at Evolve BioSystems.



process that spanned over two decades and involved a global panel of industry and academic experts.[9] So beware, sudden name changes and reclassifications may not be innocuous and should be investigated closely. When in doubt, contact the manufacturer and enquire about the change.

2. Check the CFU and "Best if Used by Date"

CFU stands for colony forming units and is the measure of the number of viable bacterial cells by plate count. CFUs are determined by allowing the organism to grow on appropriate media under controlled conditions and then counting the number of colonies present. This method is a long-standing industry standard and is the notation recommended by the US Food and Drug Administration for probiotic labels.[10] Quantities can vary but are typically in the millions or billions per unit. Most importantly, the CFU should be explicitly indicated for each individual strain contained in a product rather than the sum of all bacterial strains. Listing a total CFU as a total would be the equivalent of listing the total vitamin dose in a multivitamin product without a dosage breakdown for each individual vitamin. Clinicians need to know exactly what and how much of an active ingredient is going into their patients. Furthermore, the CFU should be guaranteed until the end of shelf life or best by date. Avoid products listing CFU at the time of manufacturing. Remember, probiotics are living bacteria; exposure to light, heat, oxygen, and moisture can reduce viability. Having a guaranteed CFU through the best if used by date ensures the probiotic contains the recommended amount of viable probiotic bacteria at the time of use.

3. Carefully review the list of ingredients

Ingredients should be listed in descending order by weight. In addition to the probiotic microorganism, product formulations often include inactive ingredients added for packaging and feeding purposes, and to protect the bacteria. Review this list and also check the "Other Ingredients" section to confirm that the product only uses ingredients known to be safe in infants.

4. Check the label for clear instruction of use and storage

Probiotic products come in many different forms, including most commonly capsules, powders, and liquids. Each form has specific requirements and instructions for use and storage. Liquid products are preferred for the hospital setting to avoid cross-contamination from aerosolized powder,[11,12] and low temperature storage protects the bacteria and extends the self-life. Make sure instructions are easy to follow and compatible with the protocols set in place in your unit.

5. Manufacturer's identification and contact information should be provided

The product label should contain manufacturer information and a direct line of contact. This information allows clinicians to choose a probiotic product from a company with knowledgeable scientists and implementation specialists that can help incorporate the probiotic seamlessly into standard of care protocols and provide continued training and support.

In summary, when it comes to quality and efficacy, the probiotic product should be able to coherently speak for itself. Accurately labeled products, containing high-quality microorganisms, robust supporting science make the best choice for your infant patients. Clinicians face a number of challenges when caring for vulnerable infants. Concerns about product quality should not be one.

References

1 Merenstein et al. 2019. "More Information Needed on Probiotic Supplement Product Labels." *Journal of General Internal Medicine* 34: 2735.

2 McFarland et al. 2018. "Strain-Specificity and Disease-Specificity of Probiotic Efficacy: A Systematic Review and Meta-Analysis." *Frontiers in Medicine* 5: 124.

3 Duar et al. 2020. "Comparative Genome Analysis of *Bifidobacterium longum* subsp. *infantis* Strains Reveals Variation in Human Milk Oligosaccharide Utilization Genes among Commercial Probiotics." *Nutrients* 12: 3247.

4 Frese et al. 2017. "Persistence of Supplemented *Bifidobacterium longum* subsp. *infantis* EVC001 in Breastfed Infants." *mSphere* 2: e00501

5 Henrick et al. 2019. "Colonization by *B. infantis* EVC001 modulates enteric inflammation in exclusively breastfed infants." *Pediatric Research* 86: 749.

6 Chapman et al. 2012. "*In vitro* evaluation of single- and multi-strain probiotics: Inter-species inhibition between probiotic strains, and inhibition of pathogens." *Anaerobe* 18: 405

7 van den Akker et al. 2020. "Probiotics and Preterm Infants: A Position Paper by the European Society for Paediatric Gastroenterology Hepatology and Nutrition Committee on Nutrition and the European Society for Paediatric Gastroenterology Hepatology and Nutrition Working Group for Probioticsand Prebiotics." *Journal of Pedriatric Gastroenterology and Nutrition* 70: 664.

8 Lewis et al. 2015. "Validating bifidobacterial species and subspecies identity in commercial probiotic products." *Pediatric Research* 79: 445.

9 Zhen et al. 2020. "A taxonomic note on the genus *Lactobacillus*: Description of 23 novel genera, emended description of the genus *Lactobacillus* Beijerinck 1901, and union of *Lactobacillaceae* and *Leuconostocacea*." *International Journal of Systematic and Evolutionary Microbiology* 70: 2782-2858.

10 Food and Drug Administration. 2018. "Draft guidance for industry: policy regarding quantitative labeling of dietary supplements containing live microbials: guidance for industry."

11 "CDC, FDA advise against powdered formula in NICUs." *AAP News* 20: 219