## LETTER TO THE EDITOR

### SUPPORTING A HEALTHY MICROBIOME AND PATIENT OUTCOMES WITH PROBIOTICS

Dear Editor:

Our understanding of the microbiome, the importance of microbiome-host interactions, and the role of dysbiosis in the etiology of specific conditions and diseases has evolved rapidly over the past 10 years. With this has come an ever-increasing number of interventions aimed at manipulation of the microbiome[1] to improve health status. Chief among these are probiotics, live microorganisms that, when administered in adequate amounts, deliver a health benefit to the host. Probiotics have been recognized for over one hundred years.[2] Use of probiotics in clinical practice is hampered, however, by a lack of strain-specific data sets including dose response and clear links to mechanism, as well as misinformation about probiotic products and therapeutic uses.[3] As use of probiotics grows beyond general claims of gut health to more targeted health claims, so too does the onus on producers of probiotics-containing products to meet rigorous standards of scientific evidence as defined by regulatory agencies.[4,5] The evidence should include, but is not limited to, full genetic characterization of the microorganism, evidence of adhesion to epithelial surfaces, data to support potential mechanism of action, efficacy, and the clinically effective dose.[6] Probiotics may impact intestinal and general health via a number of different mechanisms including by: providing a competitive disadvantage to potentially pathogenic microbes, directly interfering with the adhesion of pathogenic microorganisms to the epithelium, helping to maintain epithelial barrier function and integrity, and modulating the immune system.[6]

Determining a clinically effective dose (potency) for administration of a probiotic can be challenging, as dose range–finding studies have typically not been undertaken in this field. Dose selection in clinical studies often represents a "best guess" by the researchers. In practice, there is often the erroneous perception that "more is better." However, potency of a probiotic is dependent upon more than just the declared number of colony forming units (CFUs) in the package. Potency will be impacted by several factors, including ability to survive gastric acids and bile and ability to colonize and adhere to the intestine, and should be selected based upon the demonstrated effectiveness in a clinical setting.[7] In addition, consideration should be given to the ability of the probiotic to survive manufacturing processes. Water activity and temperature sensitivity can impact the long-term viability of probiotic microorganisms. Shelf-stable products are appealing for their perceived ease of use and improved patient compliance. Room temperature stability (or "shelf stability") results from a combination of strain selection (low water activity, high temperature sensitivity, intestinal colonization efficiency) and optimized processing and packaging procedures. Of note, the number of CFUs stated on the label reflects the number guaranteed at the end of shelf life.

Our understanding of the impact of probiotics in health and disease will likely be fueled by discoveries from the ongoing microbiome project and complementary work by leading global clinical research institutions. By understanding the underlying science of individual probiotic strains, specific clinical effects, effective dose, and label information, consumers and healthcare providers will be able to more effectively choose the probiotic(s) that is likely to result in the greatest health benefit. The development of targeted strains for specific clinical indications represents the new frontier in probiotics research, thereby providing reliable, quality healthcare solutions.

*Nikhat Contractor, PhD*
*Andrew G. Swick, PhD*
*Michael B. Montalto, PhD*
*John P. Troup, PhD*
Gig Harbor, Washington

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