Probiotics—The quality challenge
NEC White Paper

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UNDERSTANDING PROBIOTICS
Although a probiotic microorganism itself is fairly simple, its role in the body is more intricate. According to Harvard Health, an estimated 100 trillion microorganisms, representing more than 500 different species, inhabit every normal, healthy bowel.

Probiotics primarily produce lactic and fatty acids in the gut, resulting in a lower pH, which help to keep other gut-dwelling microbes in balance. Considered good bacteria, these microorganisms generally don’t make us sick, but instead are helpful and provide various health benefits, with the most studied benefit, being the prevention of diarrhea.

The microorganisms in probiotic dietary supplement products are similar to our bodies normal microbial flora. This allows supplementation to be a viable option when there is a potential imbalance in the body. While the body generally does a good job maintaining a healthy bacterial balance, certain situations such as antibiotic use, traveling extensively or even long-term exposure to stress can create the perfect conditions for an imbalance.

Finding a quality probiotic supplement might seem like an easy undertaking as the grocery aisles and supplement stores are lined with multiple options, packaged in eye-catching containers, promising various health benefits. But in reality, quality probiotics, which have a live Colony Forming Unit (CFU) count up until expiration, aren’t easily recognized as the manufacturing process is generally unknown to the average consumer. Probiotics require an advanced level of consideration and handling during the formulation and manufacturing process, to ensure that finished products meet label claims and shelf-life.

FORMULATING FOR SUCCESS
For a finished probiotic to be successful, there are many considerations that must be addressed before it ever goes into production. Starting with high quality strains from reputable probiotic suppliers, is a vital first step in creating an efficacious finished product that meets shelf-life expectations. Contract manufacturers should verify vendor CofAs through testing, confirming incoming probiotics for viability. This is an essential step that is worth the time and money, and can prevent product failures later.

Probiotic products should be formulated with the appropriate ratio of ingredients to achieve optimum machine run-ability. A master formulator will take into account the ratio of ingredients to address both homogeneity and ingredient flow. For instance, too much of certain prebiotics combined with a probiotic, can create flow issues. These factors can create delays in completion or possibly require reformulation which can affect the product.
label and marketing material. Every aspect of the finished product, either capsule, powder or tablet, should be carefully considered during formulation to ensure success.

Since probiotics are live microorganisms, they must be formulated with ingredients that have a low water activity. One of the most detrimental factors to probiotic survival is moisture. According to a recent study, Lactobacillus rhamnosus GG (LGG) was prepared with a crushed flaxseed matrix with three different water activities being used. These mixtures were stored at room temperatures for 14 months and then tested for viability. It was determined that the mixture with the lowest water activity/\(a(w)\), had the least reduction in viability over time\(^4\).

Formulators must also consider the finished product packaging and what types of moisture barrier the product will be in contact with. Bottles, pouches, stick pack film and shrink material all have moisture barrier specification factors that will contribute to the product’s stability.

Shelf-life is also a major aspect for formulators when developing a probiotic product. Over-formulating with conventional strains to ensure CFUs meet label claims at product expiration, is an economical approach when creating a typical 12-month shelf-life probiotic product. Although at an added cost, extended shelf-life probiotics such as spore-forming and microencapsulated, offer many benefits to marketers and end-users. Extended shelf-life strains can withstand many common factors which adversely affect probiotics such as humidity and temperature. And while the average probiotic supplement shelf-life is 12 months, an extended shelf-life probiotic product can last up to 24 months.

THE MANUFACTURING CHALLENGE

A superior probiotic product is the end result of every established manufacturing process being completed to specification without shortcuts. Probiotics should always be handled under appropriate storage conditions. Special refrigerated units which are maintained below 4 °C, are used to help ensure viability. This can be a costly addition to a manufacturing facility, but this level of storage is critical for probiotic survival.

Special challenges also need to be addressed in the manufacturing environment as temperatures and humidity must be kept low when handling probiotics. Temperatures should not exceed 22 °C during processing and humidity levels should be less than 30%. Probiotics should also be allowed to acclimate to room conditions before handling. These factors can make or break the probiotics’ level of activity over time.

Probiotics, like all dietary supplements, are required to meet label claims to be FDA-compliant. To achieve this, their specific activity or CFUs, must be maintained until the end of their shelf life. Exposure to moisture or high temperatures during the manufacturing process will result in a rapid die off of the microorganisms once they hit the store shelf. This type of carelessness during the manufacturing process can produce an inferior product that is of poor value to consumers.

The final consideration is cross-contamination and how the manufacturing environment in general can be affected. Facilities working with probiotics should have heightened and rigorous cleaning procedures, with an established quality control protocol to continuously verify the environment has been effectively cleaned prior to continued manufacturing. Unfortunately, it takes only micrograms of highly concentrated probiotic material to fail a non-probiotic finished product. And while not harmful, cross-contamination will fail the product during testing.

If manufacturers employ dual-purpose production rooms, managing probiotic quality control procedures requires a specific approach. Scheduling probiotic products at the end of the day, followed by a full wash-down of the room and all equipment,
can prevent cross-contamination of other products. Because of probiotic cleaning requirements, a verification step is required after cleaning has been completed. This is accomplished in two steps, with the first being a visual inspection to ensure there is no residual product on equipment. Secondly, ATP (Adenosine Triphosphate) swabs can rapidly detect residual proteins, and verifies if the cleaning processes were effective.

**TESTING—THE MOMENT OF TRUTH**

Following the correct procedures and taking careful and deliberate measures during manufacturing is critical, but superior probiotic products will pass one final step— finished product testing. A manufacturer should be cautious on which lab they use to test their probiotic products as not all labs are created equal. Choosing a lab that is accustomed to handling probiotic material and performing specialized testing with accuracy, can be challenging as there are very few labs who excel in probiotic assays.

Just as in the manufacturing process, probiotic testing has challenges. Quantifying probiotics is accomplished by testing the living bacteria. There are many species of probiotics, each requiring a specific growth medium. It is important for the testing lab to understand the growth requirements for optimal recovery.

The lab environment is also at risk for cross-contamination as probiotic bacteria can pollute a microbiology clean environment. To mitigate this risk, the lab will pay close attention to air quality and cleaning procedures, utilizing a segregated area for sample preparation.

Testing represents a costly step which some manufacturers may not be willing to absorb in the interest of producing economical, but possibly inferior products. While producing a superior probiotic can be cumbersome and costly, there is never a reasonable excuse for allowing an inferior product to go to market. Consumers trust that what they purchase and ingest will be safe and do what it claims. Knowledge is key when it comes to understanding how a quality probiotic product is made, and awareness can only help raise the bar and strengthen the dietary supplement industry.

References