Dr. Ms. Cheryl McRae
Branch Head
Complementary and OTC Medecines Branch
Therapeutic Goods Administration (TGA)
Canberra ACT 2601

September 8, 2023

Dear Madam

The **International Probiotics Association (IPA)** is a global non-profit organization bringing together through its membership, the probiotic sector's stakeholders including but not limited to academia, scientists, health care professionals, consumers, industry and regulators. The IPA's mission is to promote the safe and efficacious use of probiotics throughout the world. Holding NGO status before **Codex Alimentarius** and observer status at **ISO**, the IPA is also recognized as the unified "Global Voice of Probiotics" around the world.

IPA would like to provide comments related to the consultation on the proposed Guidelines for the Quality of Listed Probiotic Medicines. IPA respects TGA's underlying motivations behind this guide and the objective to provide consumers with products of quality. However, IPA is concerned about certain elements that, if understood correctly (e.g. quantification at strain level), could heavily impact the sector and unnecessarily disrupt the market, which goes in the opposite direction of TGA's intentions towards consumers. This would spread confusion and creates an unlevelled playing-field between single-strain products and probiotic blends, noting that several scientific and expert opinions support the benefits blends of probiotics could offer, as well as single-strain ones. Because current methodologies do not consistently allow for the quantification of different strains in a product, such regulatory requirement would cut out of the market hundreds of these probiotic blends that are safe and efficacious, and most importantly are needed and already trusted by Australians.

The probiotics industry continues to work and invest on the topic of quantification at the strain level in the finished product, the advancements are noticeable, however, the industry is not there yet. Best practice currently remains as quantification of strains by input and overall quantification in final products. This approach is currently adopted and recognized by several competent regulatory authorities around the world. It is aligned with the body of literature for probiotics that was built over a century using blends which reported total microbiological counts (not at the strain or genus level). Consumers have used and relied on these products as produced, documented and labelled throughout all these years. It is difficult to visualize what additional and truly useful information would be given to the consumer by quantification at the strain or genus level.

IPA recommends an extreme caution to be taken before implementing these regulatory requirements, especially without proper scientific and regulatory consultation across the globe. In our opinion, these requirements will significantly modify the market without necessarily bringing an added value.

According to the technologies available today, methodologies used worldwide at the highest quality level are a combination of precise quality management using quantification by input and total enumeration tests. In particular, probiotic producers generally guarantee the identity, stability and purity of their production according to the establishment of a validated Master Cell Bank, Working Cell Bank and deposit of the strain in the international collection. Each single production is made using a seed-lot system where each time a new vial of the same clonal strain is used for a new production. Quality by input imposes the tracking of each single input using the metric required by the product labelling. After mixing, the blend is tested for potency to verity that the number of cells is within specification. Similar approach is used for Identification. The manufacturer of the probiotics strains conducts a thorough genotypic, phenotypic and characterization profile of the strain, then follow the good manufacturing practices and traceability as described above. After mixing the strains together, phenotypic methods can be used. Although the responsible industry is working on techniques that would allow identification and quantification of each strain in a blend, the industry is not yet at the stage to adopt these emerging techniques in a practical way. While works continue, IPA also find that these current limitations must be taken into consideration, as well as their impact on the industry. A contract manufacturer in Australia receiving a blend of strains, can be interpreted as the blend being the ingredient that can be verified by phenotypic methods and quantified as a total blend. This practice should be considered acceptable provided the supplier is carefully selected and qualified and is compliant with good manufacturing practices. This practice is widely accepted by competent authorities overseas.

The above-mentioned limitations similarly apply to stability, where stability of every strain within a blend is far from being possible in a practical way thus the finish product's total count should be sufficient to substantiate stability provided the practices described above (quantification by input, GMPs, etc.). Again, applying such random requirements would result in the extreme limitation of choices of products favoring single strain products and that is totally unfair and a pity towards the consumer choice of products.

IPA urges TGA to accept the limitations of current technologies, take into account the long history and literature, measure the risk that will result in a dramatic destruction of the Australian market, penalizing Australians as compared to other consumers in the world such as, and not limited to, Canadians, Americans and Europeans, where the regulatory framework allows for blends and single strains and such differential quantification is not a requirement nor is a limitation. A good example, is, Health Canada - where Natural Health Products definition and provisions mirror complementary medicine in Australia – acknowledge technologies limitations and equally regulate probiotic mixtures and single strains.

Our Scientific and Regulatory Committees are at TGA's disposal for any discussion on the matter of quantification or any probiotic-related topic. It is crucial to keep communication ongoing and accordingly understandings and interpretations harmonized. Per instance, a medicine containing probiotic and postbiotic ingredients should not be considered a synbiotic medicine as reported in section 2. A synbiotic is commonly referred to as a mixture of prebiotics and probiotics rather than postbiotics and probiotics. Such proposals without further discussion would bring confusion to the consumers. Similarly, only listing strain designations on labels is not a common labelling practice (as figure 2 suggests). IPA recommends species and strains to be always labelled, allowing consumers to compare products and make informed purchasing choices. Such practices will promote consumer education and avoid confusion. It is also important confusion be mitigated at manufacturing levels by using common terms, such as "concentration" rather than "strength" when referring to the therapeutic effect (Section 3.1 Figure 1).

In conclusion, IPA appreciates the opportunity to contribute to this consultation initiative, and we remain available to provide clarification regarding the contents in this letter. We aim to continue the dialogue with the TGA and are grateful of TGA's transparency regarding the probiotics sector.

Thank you and my sincerest regards,

[redacted]