Bacillus subtilis HU58™

The benefits of probiotics your customers demand, delivered with superior stability!

Health & safety backed by 100 years of biosolutions expertise

What is *Bacillus subtilis* HU58™ ?

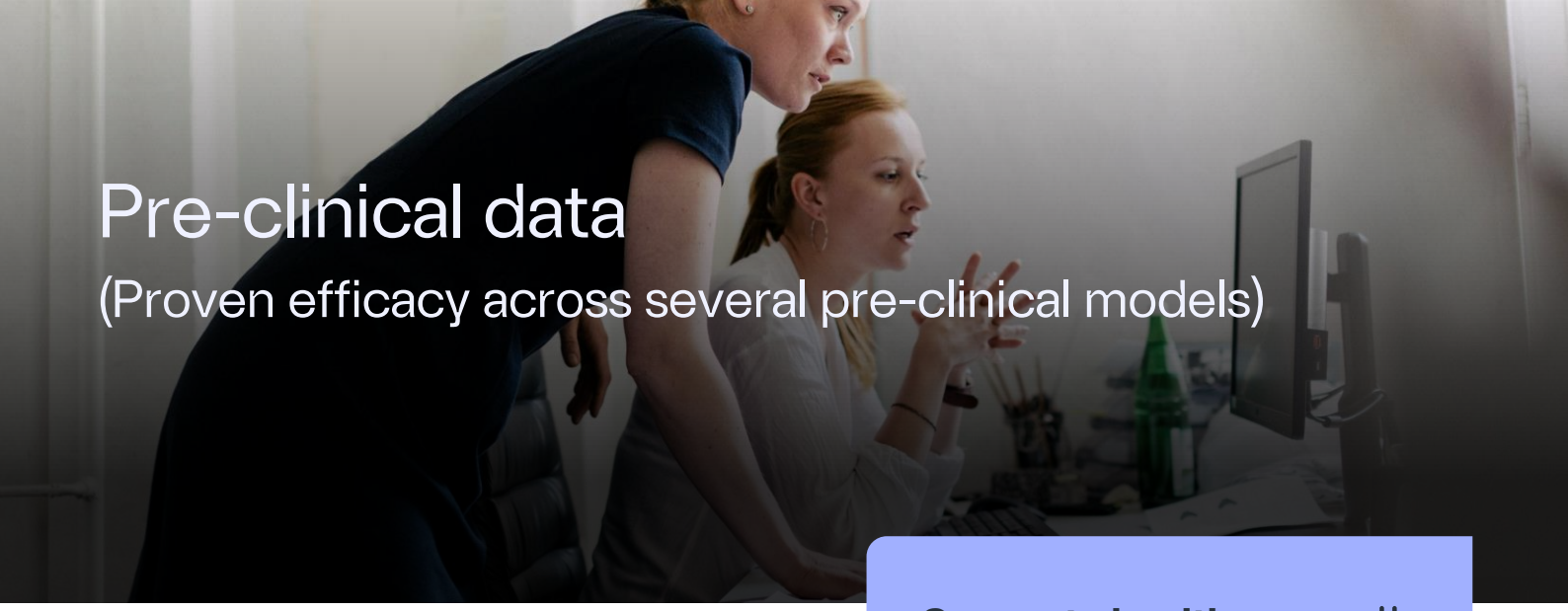
Bacillus subtilis HU58™ is a unique probiotic strain supported by a significant amount of preclinical, clinical, and safety studies. This strain has an established history of safe use as part of the successful Megaspore® blend and is now offered as a single ingredient probiotic product.

HU58™ is formulated in a protective spore form that has been shown to survive the acidic environment of the stomach. It then germinates and grows in the gastrointestinal tract, effectively colonizing the gut. This strain produces beneficial metabolites that support a healthy gut.

HU58™ is stable through various food production processes such as HTST pasteurization, hot water applications, and many others. Once formulated into a food or beverage, HU58™ can help you achieve probiotic stability through the shelf life of your product.

What are the benefits of HU58™ ?

- In pre-clinical and clinical studies, HU58™ has been shown to provide benefits related to digestive health, gut microbiome support, and immune health. Research on HU58™ has been shown to benefit multiple aspects of digestive health including relieving occasional upset and intestinal integrity.
- HU58™ has been demonstrated to be safe and efficacious in multiple study populations. Additionally, HU58™ has been on the market for a decade either as a single strain probiotic product or as part of probiotic blends.



Pre-clinical data

(Proven efficacy across several pre-clinical models)

Adapted to survive in the human intestine

- HU58™ germinates from spores into vegetative cells and proliferates in the gastrointestinal (GI) tract of mice (Tam et al., 2006).
- Isolated from healthy volunteers, HU58™ was confirmed to grow in the anaerobic conditions of the human GI tract (Hong et al., 2009a,b).
- Survives the acidic environment of the stomach and persists up to 2 weeks in the mouse gastrointestinal tract (Permpoonpattana et al., 2012).
- Produces a surfactant biofilm which facilitates robust growth and may promote adherence to the mucosal epithelium enabling longer persistance in the GI tract (Permpoonpattana et al., 2012).
- Survives and maintains cell count under extreme conditions including (i) long-term storage at ambient conditions, (ii) simulated Galactic Cosmic Radiation and Solar Particle Event radiation provided by the NASA Space Radiation Laboratory, (iii) exposure to simulated gastric fluid, and (iv) exposure to simulated intestinal fluid (Fajardo-Cavazos et al., 2021; Possemiers et al., 2013).

Supports healthy gut microflora

In the *in vitro* simulation of the human gastrointestinal tract model, M-SHIME®, HU58™ has been shown to modulate both the healthy and disrupted gut microbiota. HU58® is capable of fermenting dietary starches into short-chain fatty acids (SCFAs) such as butyrate, acetate, and propionate, which have protective effects towards the intestinal epithelium (Possemiers et al., 2013; Mesnage et al., 2021; Duysburgh et al., 2019).

Supports healthy immune function

- HU58™ has the capability to stimulate proliferation of immune cells associated with the gut, activating a potent innate immune response (Huang et al., 2008).
- Increases anti-inflammatory IL-10/IL-12 ratio to a level similar to or higher than other commercially available Bacilli species (unpublished internal data).

Clinically proven efficacy

(Proven efficacy across several clinical trials)

Supports healthy gut microflora

- In an open-label study using antibiotic-associated diarrhea (AAD) as a model for GI upset, HU58™ reduced the duration of AAD and significantly improved stool quality in comparison to placebo (Mehta et al., 2020A).
- Gut microbiome balance can influence levels of ammonia, an undesirable metabolite. In an open-label study, HU58™ supplementation showed significant reduction in blood ammonia level in participants with an elevated baseline level (Yossef et al., 2020).

Supports healthy immune function

- An open-label study in healthy adult individuals demonstrated that HU58™ induced a 45% reduction of pro-inflammatory marker IL-6 and a 55% reduction of pro-inflammatory marker, TNF-α (Dound et al., 2017).

Strong safety profile of the HU58™

The *B. subtilus* HU58™ strain has been on the market since 2013, has been tested in 8 clinical trials and both a 60 and 28-day oral toxicology study was conducted. The strain was shown to be well tolerated and there were no adverse events reported. Hence, there are no safety concerns in the consumption of the strain (Thao et al. 2011; Gatne et al., 2014 (unpublished)).

This strain has also been studied in conjunction with complementary strains for additional benefits:

As part of MegaSporeBiotic® and/or MegaDuo®, HU58™ may support improvements in metabolic health

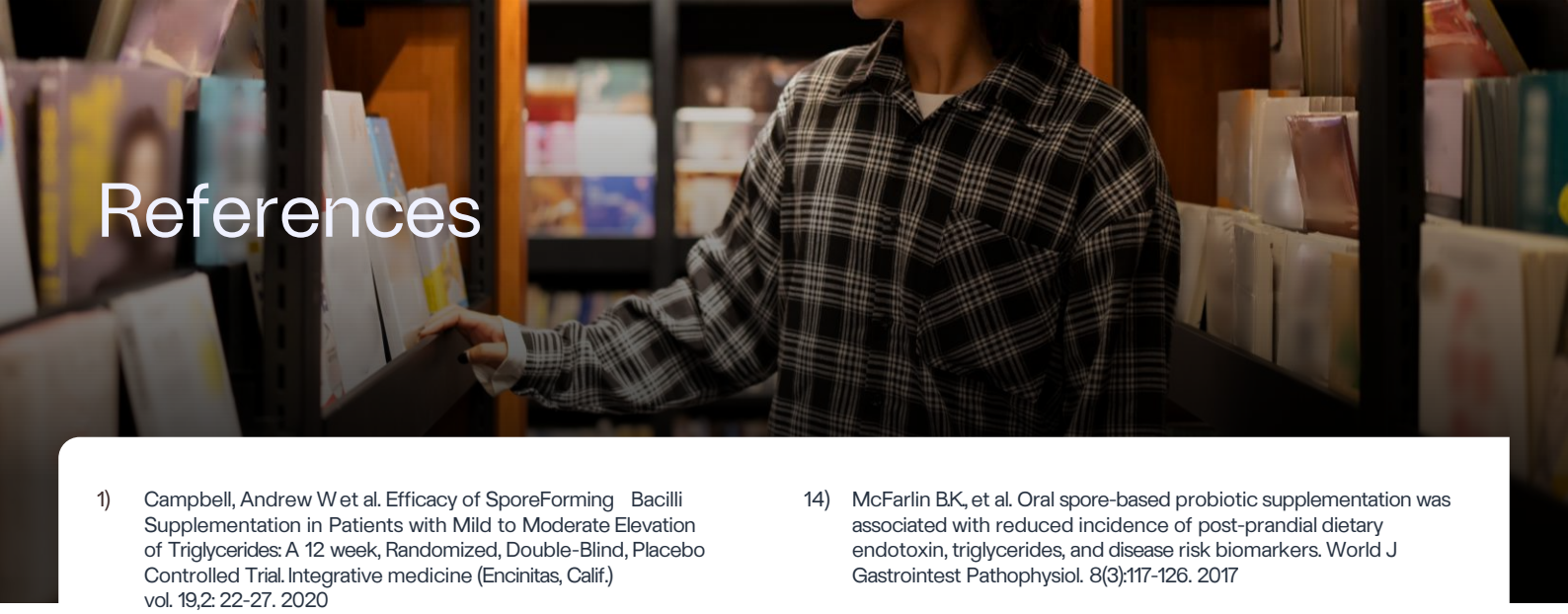
- In a trial of college-age subjects with dietary endotoxemia Megasporbiotic® supplementation reduced triglycerides, proinflammatory cytokines (IL-12p70 and IL-1β), and associated post-prandial dietary endotoxin levels (McFarlin et al., 2017).
- In adults with hypertriglyceridemia, the probiotic blend decreased non-fasting triglyceride levels compared to placebo (Campbell et al., 2020).
- In a small study in obese/overweight individuals, the MegaDuo® probiotic blend plus prebiotic induced a 35% reduction in visceral fat (the fat around organs) compared to those on placebo (McFarlin et al., 2022).

As part of MegaSporeBiotic, HU58™ may support healthy skin

- In a study in healthy participants with and without acne, the probiotic blend improved total, noninflammatory, and inflammatory lesion counts in those who had acne compared to those on placebo (Rybak et al., 2023).

As part of MegaSporeBiotic® and/or MegaDuo®, HU58™ may support healthy digestive function

- As part of MegaSporebiotic®, HU58™ has been shown to have clear anti-inflammatory properties across several animal models (the acetic acid-induced colitis model (Catinean et al., 2020), a liver inflammation model (Neag et al., 2020) as well as in a *Clostridium difficile* (CD) rodent model (Kapourchali et al., 2020)).
- As part of MegaSporebiotic®, HU58™ has also been shown to strengthen the intestinal barrier by normalizing the tight junction protein expression (Neag et al., 2020; Kapourchali et al., 2020). Tissue damage has also been shown to be reduced in rats with induced colitis (Catinean et al., 2020).
- As part of MegaDuo®, the strain was shown to protect against intestinal membrane damage in an *in vitro* immune/epithelial cell line model of antibiotic induced gut barrier damage (Marzorati et al., 2020).
- As part of MegaDuo®, HU58™ has shown efficacy in resolving the symptoms of AAD such as above-normal stool frequency and consistency along with pain in abdomen, sensation of bloating and flatulence (Mehta al., 2020B).
- Children treated with a syrup containing MegaDuo® showed significant improvement in stool consistency and duration of diarrhea over placebo syrup (Dhongade et al., 2022).
- As part of MegaSporebiotic®, HU58™ has been shown to improve IBS symptom severity and the quality of life in subjects. The probiotic blend was also shown to be as beneficial in IBS patients as a low FODMAP diet or antibiotics (Catinean et al., 2019).



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