

# UltraProbiotic

## Goal

To supply eight strains of the two most studied and used live microorganisms (probiotic), Lactobacillus and Bifidobacterium in adequate amounts (35 billion per capsule) to improve the natural balance of beneficial gut bacteria often disturbed by lifestyle and environmental factors. Proper use may help establish (re-colonize) and maintain the user's intestinal microbial system to support the health and function of the gastrointestinal (GI) tract and subsequently other important systems of human health. Desired outcomes from establishing a healthy gut microflora include proper GI tract functioning and continued integrity to achieve proper digestion and related nutrient synthesis and absorption. A healthy gut microflora may also have a positive influence on body composition and other important health parameters such as preventing or shortening illness through immune and GI system enhancement and/or competitive inhibition of pathogens.

## Rationale

Good and bad bacteria exist in the human gut and it is important that the beneficial bacteria remain the dominant strains in order to support overall intestinal function<sup>1</sup> and human health.<sup>2,3,4</sup> Diet, natural ageing and lifestyle, including intense exercise and other stresses, can upset the proper bacteria harmony to a point where GI tract problems develop which can trigger other negative health outcomes.<sup>5,6</sup>

Probiotics are live microorganisms, which when proper strains are administered in adequate amounts, may offer health benefits to the user by restoring the balance in favor of the good bacteria.<sup>5,6,7,8,9,10</sup> The probiotic strains most commonly used are from *Bifidobacterium* and *Lactobacillus* (like other microbes, probiotics are defined by their genus [e. g. Lactobacillus], species [e. g. L salivarius], and strain name [L salivarius UCC118]).<sup>11,12</sup> These groups of strains have the ability to resist the physicochemical environment of the digestive tract helping them to deliver the desired beneficial microflora balance.<sup>13</sup>

The small intestine is a primary target for probiotic intervention because of its concentration of immune cells and because its health is central to that of the entire body.<sup>14</sup> Additionally, lactobacilli are not dominant in the small intestine, so probiotics can cause a significant microflora shift that can't be achieved in the overcrowded colon.<sup>15,16</sup> In a landmark study, Van Baarlen, et al. gave healthy men the probiotic lactobacilli and documented a mucosal transcription response in the small intestine, with 300-750 genes affected in a strain-specific manner demonstrating the complexity of identifying mechanisms of action for specific health outcomes.<sup>17,18</sup> From a clinical standpoint, further complicating matching probiotics to sickness symptoms or cause of disease, is the individual variability of existing resident microbiota, which is continually subject to genetic, diet, exercise and environmental/lifestyle factors.<sup>19,20,21</sup>

Additionally, these confounding factors contribute to the considerable differences in people's responses to any probiotic intervention. Study subjects may be healthy but differ immensely in the molecular makeup of their mucosa, suggesting that various solutions for health are possible and thus influence the responsiveness to a specific probiotic treatment, which probably partially explains 'non-responders' in probiotic trials.<sup>10,22</sup>

Notwithstanding the above, there is a general consensus in the scientific community that probiotic interventions can play a role in preventative health care<sup>10,23</sup> and in limited clinical applications such as in acute gastroenteritis,<sup>24,25</sup> diarrhea,<sup>26</sup> and body fat related diseases.<sup>2,4,27</sup> The support for the dotFIT UltraProbiotic is limited only to its potential to help establish or maintain a favorable gut microbiota that would in turn impart related health benefits. Therefore, there will be no discussion around probiotic clinical applications other than a related potential mechanism of action.

## Lactobacillus

Lactobacillus refers to any long, slender, (gram-positive) rod-shaped, anaerobic bacterium of the same genus that produces large amounts of lactic acid in the fermentation of carbohydrates.<sup>28</sup> Lactobacilli are symbiotic and comprise



part of the approximate 400 normal flora in the human gastrointestinal, genital and urinary tracts<sup>29,30</sup> Lactobacilli are present in breast milk and many fermented food products (e.g. yogurt, kefir, etc.) as well as in capsule form.<sup>31</sup> Among others, specific lactobacillus species include Lactobacillus acidophilus, bulgaricus, rhamnosus, salivarius and Lactobacillus plantarum.<sup>32</sup>

## Bifidobacterium

Bifidobacteria are another species of "good" bacteria that live in a healthy intestinal tract. Unlike lactobacillus, bifidobacteria are strictly anaerobic (don't survive in oxygen rich environments).<sup>33</sup> Like lactobacillus, they are rod-shaped, gram-positive bacteria that belong to a group called lactic acid bacteria that normally colonize in the GI tract (primarily the colon area).<sup>34</sup> While bifidobacteria and lactobacillus share similar mechanisms of action in supporting the health of the GI tract, bifidobacterium appear to be the most important organisms for providing a microbial barrier to infection as they produce antimicrobial substances that have activity against invading unwanted organisms.<sup>34</sup> Bifidobacteria contribute to the health and function of the GI tract and act to alleviate or aid in the prevention of infectious disease through similar (e.g. effects on the immune system, resistance to colonization by pathogens, etc. - see below) and unique pathways and regions of the GI tract, for the same potential health results.<sup>35</sup> Therefore bifidobacteria strains (e.g. lactis, bifidum, longum) of probiotics are most often given in combination with lactobacillus.<sup>10,11,12,13,40</sup>

#### Lactobacillus and Bifidobacterium in Probiotic Supplementation

By administering probiotics made up of strains from the two most common good bacteria genus, lactobacillus and bifidobacterium, the goal is to mimic the actions that a healthy gut flora (microbiota) normally produces for the host as described throughout this section. Although consumption of probiotics has some impact on the immediate composition or diversity of the current resident microbiota, studies now show probiotics may have greater influence on gene expression and metabolic activity of the microbiota, suggesting these actions may be the major contributor of the potential health benefits of probiotic supplementation.<sup>10,17,18,36,37</sup> In other words, it is now known that probiotic metabolites and signaling from the microbiota as a whole provide nutritional, trophic, metabolic, and protective input to the development and maintenance of the digestive, immune, and neuroendocrine systems.<sup>10,17,18,36,37</sup> Because the main potentially health-enhancing bacteria are the bifidobacteria and lactobacilli, both are contained in the UltraProbiotic and all further discussion (unless specifically called out) considers both genuses collectively since they have common and unique contributions and both are present in adequate amounts to deliver the desired goals.

#### **Basic Mechanisms of Action**

Probiotics, (opposite of antibiotics, which can also kill off good bacteria) such as lactobacilli, are "friendly bacteria" that are used to re-colonize parts of the body where they should normally be present to help maintain a healthy intestinal tract.<sup>10,26</sup> The human body depends on the healthy balanced colonization (predominately-friendly bacteria) of gut bacteria for multiple functions including absorbing and manufacturing of specific nutrients,<sup>38</sup> metabolizing foods, immunological benefits<sup>5</sup> and prevention of colonization by pathogenic (bad) bacteria.<sup>39</sup> Lactobacilli also appears to deliver nutritional benefits including inducing growth factors while increasing the bioavailability of minerals, stabilizing the mucosal barrier, and decreasing intestinal permeability.<sup>10,40,41</sup>

#### **Pathogen Inhibition**

Lactobacillus and Bifidobacterium supplementation is often used to re-colonize depleted normal flora to treat or help prevent pathogenic organisms from taking up residence (Figure 1) and causing disease or sickness.<sup>42,43,44</sup> Probiotics colonize the intestinal (and urogenital) mucosa and appear to prevent the pathogenic bacteria from the mucosal binding sites.<sup>10,45,46,47</sup> In the same vein, Lactobacilli is proposed to inhibit the translocation of bacteria across the intestinal mucosa by fortifying the epithelial barrier and accelerating its repair.<sup>48</sup> And finally, inhibition of pathogen bacteria may also take place from the presence of the Lactobacillus and Bifidobacterium intestinal by-product, lactic acid, which may be bactericidal to intestinal pathogens.<sup>49</sup>





Figure 1. Preventing pathogen residence in compromised or potentially compromised flora. Influx of pathogens would otherwise limit the protective signaling from the microbiota to the host; probiotic supplementation with non-specific (friendly bacteria) probiotics such as from the lactobacillus strain can populate the host and therefore block harmful bacteria from habitation (adapted from Shanahan with permission).<sup>44</sup>

#### *Immune Support*

In the intestinal tract, probiotics modulate immunity through intestinal epithelial, M-cell and dendritic cell receptor interactions. Probiotics also extend their immunity influence beyond the GI tract by interacting with the common mucosal immune system (CMIS).<sup>50</sup> The CMIS connects inductive sites in the GI tract (Peyer's patches) to important local effector sites and other mucosal surfaces such as the upper respiratory tract and uro-genital tract.<sup>51,52</sup> Probiotics may also protect against infectious diseases by several mechanisms, <sup>53,54</sup> including secretion of antipathogen substances, competitive inhibition to block invaders, maintenance of mucosal integrity and stimulation of systemic or mucosal immune responses (as described above).<sup>50,53,54,55</sup> Lactobacilli and Bifidobacterium species can produce antimicrobial substances<sup>56</sup> that are known to enhance epithelial gut barrier functions<sup>57</sup> and also stimulate cytokine<sup>53,56</sup> and SIgA, (the predominate immunoglobulin class in external excretions) an important human substance for maintaining microbiota balance and protecting the GI and respiratory tracts against pathogens.<sup>53,58,59</sup> Like other stressors, strenuous exercise clearly suppresses the immune system, <sup>60,61</sup> and therefore probiotics may benefit an athlete's or exerciser's performance indirectly by not only helping to maintain GI function and health, but also through prevention of exercise-induced immune-suppression, thereby reducing vulnerability to illness<sup>50,62</sup> in people of all ages. A meta-analysis by Hao Q et al. which examined the effects of probiotics for preventing upper respiratory tract infections (URTIs) concluded that while the quality of evidence was low, probiotics may be more beneficial than placebo for preventing URTI's.<sup>63</sup>

In newborns, the gut microbiota plays a major role in promoting and maintaining the mucosal immune system in terms of structure and function, and in the creation of a well-balanced immune response.<sup>64</sup> Intestinal-associated mucosal lymphoid tissue becomes reactive to pathogenic bacteria but acceptable to "friendly/beneficial" bacteria.<sup>65</sup> Additionally, the intestinal flora plays a crucial role in the development of tolerogenic dendritic cells from the



# mesenteric lymph nodes of the gut-associated mucosal lymphoid tissue and in the production of secretory IgA (SIgA).<sup>50,66,67</sup>

Clinical trials have demonstrated the preventive benefit of probiotics (*Lactobacillus* or *Bifidobacterium*) in pregnant women and their infants in reducing the risk of allergic diseases including atopic dermatitis,<sup>68,69</sup> which highlights one of the reasons breastfeeding may reduce the risk of child allergies. The contents of breast milk (Bifidobacterium and galactooligosaccharides) accelerates the growth of necessary friendly bacteria.<sup>70,71</sup>

In a four-month probiotic study in the elderly, Lefevre et al. showed in a subset of participants who provided biological samples, that supplementation stimulated the immune system and decreased the frequency of respiratory infections.<sup>53</sup> Jespersen et al. also found a reduction in the duration of upper respiratory system infections of healthy subjects aged 18-60 years using lactobacillus probiotics.<sup>72</sup>

#### Weight, Body Composition and Related Health Concerns

In 2011 Jumpertz et al. published an important study in which an association was found between gut microbes and nutrient/calorie absorption, indicating that the microbiota may affect energy balance and adiposity making it a potential target for treatment.<sup>73</sup> Earlier studies with mice demonstrated interplay between diet, energy balance and the gut microbial composition and its gene pool.<sup>74, 75</sup> These trials indicated that associations between the gut microbial community and obesity may be causal rather than after the fact.<sup>76</sup> To support this theory, the transplantation of a gut microbiome from obese donors into germ-free recipients resulted in a greater increase in adiposity than transplants from lean donors.<sup>77</sup> This influence of the microbiota on nutrient partitioning may be from modulating the expression of host genes (ex: suppression of the intestinal expression of a circulating lipoprotein lipase inhibitor produced in the gut epithelium may be one mechanism the gut bacteria makeup could increase fat deposition) as well as calorie absorption.<sup>73, 78</sup> Human studies have shown a correlation between obesity and the gut microbial community structure<sup>79,80</sup>, and the abundance of genes in the microbiome involved in processing diet components.<sup>94</sup> Supporting the theory of altered microbiota and weight changes are studies that demonstrated increases in Bacteroidetes (bacteria phylum [categories]), which decreases calorie absorption and reductions in Firmicutes (increases calorie absorption) with weight loss.<sup>73,81,82,83</sup> Other human studies determined that obesity is associated with low quantities of intestinal *Bacteroidetes* and reduced overall bacterial diversity.<sup>2,84,85,86</sup>

#### **Synergy of Prebiotics and Probiotics**

Studies of healthy adults showed that approximately 5% of consumed calories are lost in fecal matter and urine.<sup>87</sup> It is also known that individuals consuming high-fiber diets (e.g. prebiotic plant foods\*) have a higher stool energy loss than those ingesting equicaloric low-fiber diets.<sup>88,89</sup> Webb et al. demonstrated that obese subjects had lower fecal energy excretion when compared with lean study participants.<sup>90</sup> Further examination of gut microbiota on metabolism shows evidence exists not only for regulation of energy extraction from diet through production of short-chain fatty acids (SCFA) from indigestible carbohydrates (e.g. fiber/prebiotics), <sup>91,92,93</sup> but the microbiota may also effect energy intake and storage.<sup>94,95</sup> The gut microbiota breaks down indigestible carbohydrates producing SCFAs, which account for 5–10% of energy requirements and are crucial to colonic cell proliferation and increasing energy production.<sup>95,96</sup> Therefore, manipulation of SCFA production through administration of prebiotics which promote the growth and activity of friendly microbial species, (thus SCFA) may promote weight loss and improve metabolic parameters.<sup>95,97</sup> SCFAs administered orally or directly into the intestine reduce food intake and body weight in diabetic and healthy humans, demonstrating their component effects (butyrate, propionate and acetate) on appetite (gut peptide release) and overall metabolism.<sup>98,99,100,101</sup> Besides the effects of SCFAs on intestinal signaling and energy usage, gut microbiota can also influence gut-brain signaling through alterations in absorptive and secretory capacity of intestinal cells – i.e. nutrient sensing. A decrease in nutrient sensing can cause an increase in energy intake.<sup>102,103</sup>

\*In short, the **prebiotic** is a specialized plant fiber that beneficially nourishes the good bacteria already in the large bowel or colon. While probiotics introduce good bacteria into the gut, **prebiotics** act as a fertilizer for the good bacteria that already exists.



**Research on the Potential of Probiotics to Mitigate Health Effects of Unfavorable Body Composition** The above data and much more have led to a flurry of research around gut microbiota and body composition with its respective health outcomes, and the proposed use of probiotic supplementation to help establish a microbiota (and/or mimic the effects of a healthy microbiota) to improve health and performance. All the studies below, unless specified, used similar strains and daily amounts of probiotics of the Lactobacillus and/or Bifidobacterium genuses.

- In Nur Arslan's detailed review on the relationship between intestinal microbiota, obesity and non-alcoholic fatty liver disease (NAFLD) the author concluded that high energy diets alter microbiota and induce gut dysfunction, subsequently leading to visceral fat inflammation and systemic metabolic abnormalities. Because an obesogenic microbiota can alter liver function including fat metabolism and storage, the review suggests that probiotics may be a treatment for NAFLD.<sup>2</sup>
- Paolella et al. in a review of human and animal trials using probiotics as a treatment for NAFLD found that
  probiotics clearly affect the intestinal microbiota and subsequently, via the gut-liver axis, may improve conditions
  of NAFLD.<sup>104</sup>
- Sepideh et al. conducted a study using probiotics in 42 patients with NAFLD and related indices found probiotic supplementation reduced glycemic and inflammatory indices, thus recommending probiotics as a complimentary therapy.<sup>105</sup>
- Ahn et al. found probiotics administered over a 12-week period to subjects with hypertriglyceridemia significantly reduce triglycerides (TG) and enhanced apolipoprotein A-V (protein that helps control TG) levels.<sup>106</sup>
- Spaiser et al. gave older adults probiotics twice daily and found they produced a less inflammatory cytokine profile and showed a beneficial shift in microbiota which resembled those shown in healthy younger subjects.<sup>107</sup>
- Mikelsaar et al. showed after four weeks of probiotic supplementation that the lipid profiles remained mostly similar between placebo and treatment groups. The values of oxidized LDL (ox-LDL) and triglycerides (TG) were significantly reduced with treatment, and after eight weeks the probiotic group exhibited reductions in LDL-C, ox-LDL, TG (17 %), and all other lipid indices. Authors concluded probiotic supplementation improved lipid profiles in clinically healthy volunteers with borderline high lipid profile indices.<sup>108</sup>
- Ipar et al. tested probiotics in obese children. Both groups participated in a reduced calorie diet and increased physical activity to produce weight loss. One group added a synbiotic (probiotics and prebiotic) supplement. After 30 days positive changes in serum lipid (and total profile) levels were significantly higher in the synbiotic group. Changes in serum total oxidative stress levels before and after the intervention period were only significant in the synbiotic group. Positive changes in weight, body mass index, and triceps skin-fold thickness were also higher in the synbiotic subjects than the diet and exercise only group. This study neatly demonstrated an additive effect of probiotic/prebiotic supplementation to a standard diet and exercise program in children.<sup>109</sup>
- A similar study was done by Safavi M et al. on 70 overweight and obese children ages 8-18 using a synbiotic supplement. At the end of the study the decrease in the BMI, waist circumference, and waist-to-hip ratio were significantly greater in the synbiotic group than placebo. Additionally, the synbiotic group had significant decreases in serum triglycerides, total and low-density lipoprotein-cholesterol levels. The authors concluded that "the beneficial effects of a synbiotic supplement on controlling excess weight and some cardio-metabolic risk factors among children and adolescents can be considered in clinical practice".<sup>110</sup>
  - Note: synbiotics refer to nutritional supplements combining probiotics and prebiotics in a form of synergism, hence the term synbiotics
- Oserberg et al. found that four weeks of probiotic supplementation provided protection from body weight gain and accumulation of fat in 20 healthy young men (18-30 yrs) consuming a high fat, (55%) hypercaloric diet compared to placebo.<sup>111</sup>

In a final comment on body composition-related health as being a potential probiotic target, Paige et al. published a comprehensive review on the gut microbiota's interaction through the gut-brain axis and potential effects on energy



balance including appetite and expenditure. Their analysis establishes strong evidence that early gut microbiota changes due to western diets (high fat and sugar) can impair the gut-brain signaling axis, becoming a significant contributor to weight gain and obesity.<sup>95</sup>

#### **Exercise and Probiotics**

Exercise itself has known effects on the GI tract. Research involving elite rugby players showed that exercise increases gut microbiota diversity and friendly bacteria.<sup>112</sup> However, although chronic moderate exercise may have an overall positive GI tract influence (in complement with diet), prolonged high intensity or ultra-endurance exercise may, at least acutely, have a negative impact akin to other body stress-related GI disturbances.<sup>60,61,113,114</sup> There are relatively few studies regarding exercise and probiotics and little consensus on its overall application but there does appear to be a particular group of athletes who engage in prolonged exercise intensity who may benefit with daily use.<sup>115</sup> These athletes become highly prone to upper respiratory tract infections (URTI).<sup>50,116</sup> As noted, the most common strains used to positively influence immune function are of the lactobacillus and Bifidobacterium species.<sup>117,118</sup> Supplementation in sub-groups of these athletes has been associated with a substantial reduction in days and severity of URTI, use of cold and flu medications for lower respiratory illness, and severity of GI symptoms.<sup>119</sup> Two other studies on physically active subjects also demonstrated a positive effect of probiotic use on the incidence, but not severity or duration of URTI.<sup>120,121</sup>

Finally, in an interesting study with mice using doses of 205 million or 1.03 billion colony forming units (CFU) per kg per day for six weeks (the lower dose is the murine equivalent of a human dose of 10 billion CFUs,) of lactobacillus probiotics, researchers stated: *"We found that supplementation increased exercise performance, decreased white adipose tissue, increased muscle mass, and enhanced gastrocnemius muscle type I fiber numbers without body weight gain. These results suggest that gut microbiota contribute to the host metabolic phenotype to affect physical activity in terms of energy balance and body composition." <sup>122</sup> This study needs to translate to humans and most certainly will be an upcoming expanded field of study – the gut-muscle-axis. Indeed, a pilot study by Georges et al. supplementing exercising subjects with probiotics and protein twice daily (one serving in the morning and one after training) compared to protein only, found the probiotic group to show a trend towards increasing performance in specific outcomes (vertical jump power and peak power).<sup>123</sup>* 

In summary, apart from the potential of probiotic supplementation in support of general GI health and function, early evidence points to a possible benefit of daily use of probiotics in supporting the immune function in individuals participating in intense, prolonged endurance exercise.

### **Dosage, Forms and Delivery**

#### Dosage

When using probiotics to support the health and functioning of the GI tract as proposed here, *Lactobacillus* and *Bifidobacterium* are considered to have a safe profile and studies have demonstrated beneficial effects at daily dosages between 1 and 40-billion bacteria.<sup>10,40,53,124125,126,127</sup> Specific strains and amounts used for clinical applications are not addressed here.

#### **Form and Delivery**

Proper encapsulation of live bacteria colonies can assure a longer and safer shelf-life and ingredient stability than functional foods (stability is based on the environment the bacteria is placed in). Most importantly, properly structured capsule delivery of live organisms also appears to be the safest way to guarantee that the desired number of bacteria reach their target destinations in the GI tract including surviving the changing acid mediums.<sup>128</sup>

#### dotFIT UltraProbiotic -35 Billion Probiotics

In order to help consumers avoid the common pitfalls of identifying the proper probiotic with the greatest potential to accomplish the established goal stated above and below, Danisco raw materials of Bioenhanced Acid Resistant Strains



(BEARS) are used for the manufacturing/packaging by Reliance for this product. These specialized strains allow stable potent ingredients (pro and prebiotics) throughout the production process and all the way to the final delivery to the gut. In order to resist all the normal vagaries of probiotic processing and their safe passage through the GI tract's harsh and ever-changing pH environment, Dansico provides the most stable cultures on the market through the use of a patented polymatrix preservation system (Patent #6,653,062) to maximize stability and cell count.<sup>128</sup> Furthermore, the product contains significant ingredient overages to help maximize the potency of viable cells through the expiration date printed on each bottle. In fact, each serving starts with ~80 billion CFUs/capsule - i.e. almost 45 billion more than claimed, thus helping to assure desired live potency (minimum of 35 billion CFUs) reaches the target at any time through the product's stated shelf life. For the final assurance, third party testing throughout the product's production and completion is provided for guaranteed potency and stability by Silliker INC. Wisconsin Labs, Covance Labs, LA analytical or Chemical Solutions.<sup>128,129</sup> Finally, the product includes a prebiotic blend (see definition and mechanisms of actions above in Prebiotics and Probiotics Synergy section) to help support the growth of desired probiotics (good bacteria).<sup>91,92,93,94,95,97</sup>

## **Summary and Next Frontier**

It is clear that gut microbiota plays a major role in the health and function of the GI tract,<sup>10,130</sup> which is important by itself in facilitating proper lifelong nourishment and inhibition of pathogen residence. However, as recent discoveries mount regarding the gut microbiota's multiple pathways of impact on overall human health from womb to tomb, the use of supplementation in the manipulation of gut microbiota may go beyond simply attempting to achieve/mimic normal healthy microbiota. Now armed with the knowledge that the human gut-microbiota functions as complex organs do, the investigation into the use of specific strains for specific health and performance targets is now in full swing.<sup>10,131,132,133,134,135,136,137,138,139</sup>

In the meantime, there appears to be no downside<sup>140,141,142,143</sup> in the use of Lactobacillus and Bifidobacterium probiotic daily supplementation in the attempt to restore and/or maintain a healthy gut microbiota since the GI tract's functioning is at the core of our health, and thus performance. The upside of a proper signaling healthy intestinal tract may be endless. Furthermore, western diets and lifestyles are notorious for compromising gut micro-flora,<sup>130,144</sup> making daily supplementing of the friendly bacteria strains from Lactobacillus and Bifidobacterium possibly an important component of preventative health care. To accomplish the goal stated here, selection of only a properly formulated, manufactured and third party tested final product (as described in the previous section) is paramount to success.

#### **Typical Use**

- All adults, (unless contraindicated by an existing health condition or discouraged through qualified medical advice), trying to establish a healthy and balanced gut microflora to achieve the associated benefits of a healthy functioning GI tract (e.g. nutrient digestion, absorption, signaling, pathogen inhibition, etc.)
  - Athletes participating in prolonged high intensity or endurance activities seeking immune support
  - Those seeking to restore the natural balance of beneficial gut bacteria that may be compromised by diet, ageing, weight and lifestyle including stress
- Take one (1) capsule daily during meals or as directed by a health professional.

#### **Precautions**

Proper use of the dotFIT UltraProbiotic 35 Billion is considered safe for the general population. All strains contained in this product have been used safely across many studies in all populations.<sup>145</sup> Concomitant use of antibiotics may decrease the effectiveness of Lactobacillus and Bifidobacterium and therefore, users are advised to separate administration of antibiotics and probiotics by at least two hours.<sup>146</sup>



#### **Contraindications**

Probiotic supplementation should be avoided by people with a predisposition to pathogenic infections, such as in severe immunodeficiency and short bowel syndrome, unless under a qualified physician's care.<sup>147</sup> Although probiotics are commonly used during pregnancy or lactation, they should only be used as recommended by the attending physician.<sup>68,69,71</sup>

#### **Adverse Reactions**

Probiotics made up of the strains in the dotFIT UltraProbiotic 35 Billion are well tolerated with little known negative reactions. The most common side effect is mild flatulence that generally subsides as use continues.<sup>10,140,141,142,143</sup>

#### **Upper Limit/Toxicity**

There is no upper limit established for the use of the probiotics used in this formula.<sup>148,149,150</sup> In fact, doses at 100 times greater have been used safely in children with ulcerative colitis.<sup>151</sup>

#### **Summary**

#### **Purpose**

To supply eight strains of the two most studied and used live microorganisms (probiotic), Lactobacillus and Bifidobacterium in adequate amounts (35 billion per/capsule) to improve the natural balance of beneficial gut bacteria, which is often compromised by diet, lifestyle, common stresses and environment. Maintaining a healthy gut microbiota (good bacteria balance) can have a positive influence on all aspects of health and well-being.

- For adults, trying to establish a healthy and balanced gut microbiota to achieve associated benefits of a properly functioning GI tract such as nutrient digestion, absorption, signaling, pathogen inhibition, and immune support
- Athletes participating in prolonged high intensity or endurance activities seeking immune support

#### **Unique Features**

Eight (8) probiotic strains from Danisco, a world leader in probiotic research and manufacturing:<sup>128</sup>

- The select strains that have been cultivated under harsh conditions developing the ability to adapt to extreme changes in environment i.e. pH, temperature
- Contains the most stable cultures on the market through the use of a patented polymatrix preservation system (Patent #6,653,062) to maximize stability and cell count without refrigeration
  - Bio-enhanced Acid Resistant Strains (BEARS) ensures survivability in both low (acid) and high (alkaline) pH environments. The BEARS strains in this formula are designed to withstand the acid conditions present in the stomach during digestion without the need for an enteric coating
- Each capsule starts with ~80 billion CFUs/capsule i.e. almost 45 billion more than claimed, thus assuring desired live potency (minimum of 35 billion CFUs) reaches the intestinal targets at any time through the product's stated shelf life
- The prebiotic blend consists of FOS (food source for probiotics), and FiberAid<sup>®</sup> arabinogalactans (patented prebiotic from Lonza<sup>®</sup> that helps support the growth of probiotics)
- Third party testing throughout the product production and completion is provided for guaranteed potency and stability by Silliker INC. Wisconsin Labs, Covance Labs, LA analytical or Chemical Solutions



# **Supplement Facts**

Serving Size: 1 Vegetarian Capsule		
	Amount Per Serving	% D\
Proprietary probiotic blend (35 billio	n cells per cap)	*
Lactobacilli acidophilus		
Bifidobacterium lactis		
Lactobacilli salivarius		
Lactobacilli plantarum		
Bifidobacterium bifidum		
Bifidobacterium longum		
Lactobacilli rhamnosus		
Lactobacilli bulgaricus		
Prebiotic blend	50 mg	*
(FOS, FiberAid® arabinogalactans)		



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