Probiotic *Lactobacillus reuteri* NCIMB 30242 (LRC™) for Heart Health Benefits
Abstract

Introduction

Bile Salt Hydrolase Active Bacteria and Cholesterol Lowering

*L. reuteri* NCIMB 30242 is a Highly BSH-Active Probiotic and has been Extensively Characterized

Clinical Efficacy of *L. reuteri* NCIMB 30242 in Cholesterol Lowering

Clinical Safety of *L. reuteri* NCIMB 30242

Additional Clinical Efficacy of *L. reuteri* NCIMB 30242

Regulatory Status of *L. reuteri* NCIMB 30242

Conclusion

References

Figures

Figure 1. % above baseline for patients taking *L. reuteri* NCIMB 30242 in Yogurt Form

Figure 2. % above baseline for patients taking *L. reuteri* NCIMB 30242 in Capsule Form

UAS Labs: The Probiotic Company
PROBIOTIC LACTOBACILLUS REUTERI NCIMB 30242 (LRC™)
FOR HEART HEALTH BENEFITS

Abstract

Cardiovascular disease is a leading cause of death worldwide, and reduction in low density lipoprotein cholesterol (LDL-C) remains the primary target for intervention. Recommendations for therapeutic dietary lifestyles targeting LDL-C lowering and heart health include regular consumption of clinically-tested foods or supplements. In this white paper, we review the nonclinical and clinical safety and efficacy with bile salt hydrolase (BSH)-active probiotic Lactobacillus reuteri NCIMB 30242 (LRC™) for the support of heart health. This includes two randomized clinical studies showing significant reductions of LDL-C of 8.92% (P=0.016) in yogurt and 11.64% (P=0.001) in capsules. Other lipids and markers of inflammation were also significantly reduced. Further, we provide mechanistic insights as well as clinically demonstrated enzymatic activity of the selected microorganism. Finally, we describe the efficacy of LRC™ for other applications as well as its regulatory documentation.

Introduction

Cardiovascular disease is considered the principal global cause of morbidity and mortality by the World Health Organization (WHO, 2011). In the United States, one in three deaths occurs as a result of CVD; half of these due to coronary artery disease (CAD). Estimated costs associated with CVD and stroke in the United States reached nearly $300 billion in 2008 and are projected to triple by 2030 (Roger et al. 2012). Cardiovascular disease is a progressive disease that starts in childhood and manifests itself with aging. A number of modifiable risk factors have been identified; adopting healthy and therapeutic lifestyle habits is an important part of managing cardiovascular risk and reducing costs associated with the disease (WHO 2007; Lichtenstein et al. 2006; Grundy et al. 2004; Adult Treatment Panel III 2002). A healthy lifestyle comprises a range of habits including: maintaining a healthy body weight, regular physical activity, consuming an overall healthy diet, reducing intakes of saturated fats, trans
fatty acids and cholesterol, avoiding the use of tobacco products and routine medical check-ups for blood pressure and cholesterol (WHO 2007; Grundy et al., 2006; Grundy et al., 2004; Adult Treatment Panel III, 2002). While sharing the same facets as a ‘healthy lifestyle’, a ‘therapeutic dietary lifestyle’ also includes the regular consumption of specifically clinically-tested low density lipoprotein cholesterol (LDL-C) lowering foods or supplements.

Cholesterol fulfills multiple functions in the body, forming part of cell membranes, hormones, and detergents that solubilize consumed fats. Ingested or synthetized by the organism, cholesterol transits the digestive and vascular systems and is transported through arteries and veins to its metabolic destinations in lipoproteins, such as LDL-C and HDL-C. Elevated LDL-C (“the bad cholesterol”) is a major risk factor for CAD and is the primary target for lipid-lowering therapy (Grundy et al. 2004, Adult Treatment Panel III 2002, Grundy 2008). LDL-C has been shown to initiate and promote the progression of the disease, including plaque formation, growth, destabilization and rupture (WHO 2011, Grundy 2008). Additional risk factors or predictors of CAD include inflammatory markers such as fibrinogen (a precursor of the blood clot component fibrin), and C-reactive protein (hs-CRP, a protein that is present at high levels in inflammation). While inflammatory risk factors are of importance, targeting them for therapy is considered secondary to LDL-C (Adult Treatment Panel III 2002). Further, cholesterol lowering therapies aimed at LDL-C often reduce inflammation through interrelated or independent mechanisms.

Understanding the gastrointestinal (GI) system and its interaction with resident microorganisms may provide possible means to regulate the metabolism of cholesterol and prevent cardiovascular disease. The GI lining consists of a surface with an estimated area of the size of a football field with great access to the circulatory system due to its high irrigation. The GI tract is exposed to a multitude of resident, non-harmful, microorganisms called “the gut microbiome”, distributed throughout its length that include bacteria, fungi and viruses. The microbial genes in the gut outnumber their human counterparts by 150-fold and many of these genes help their host organism to perform metabolic functions. In fact, many essential processes that take place in the gut are performed by our resident microorganisms and would not occur in their absence. Probiotic bacteria are defined as “live microorganisms that when administered in adequate amounts confer a health benefit on the host” (WHO/FAO 2002). This definition has undergone a recent review with a slight grammatical change, resulting in a working definition of “Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host” (Hill et al. 2014).

These species may interact and alter the GI flora or release a number of molecules including enzymes that can improve digestion, metabolism, modulate inflammatory responses, stimulate the immune system, and even affect the nervous system to control pain (Hord et al. 2008). Probiotics have gained great interest among consumers of health products, physicians, and scientists, and a remarkable focus is placed in finding means to treat metabolic disease by delivery of some of these microorganisms.

Bile Salt Hydrolase Active Bacteria and Cholesterol Lowering

Bile acids are natural detergents synthesized in the liver from cholesterol, stored in the gall bladder, and released into the duodenum with the purpose of transporting dietary fat and other ingested lipophilic compounds into the circulation. Bile acids get reabsorbed in the distal ileum and return to the liver with only a small percentage being eliminated through feces. In order to improve their solubility, bile acids can get conjugated to hydrophilic compounds such as glycine, and thus form conjugated bile acids. Bile salt hydrolase (BSH) is an enzyme present in many commensal bacteria that breaks down conjugated bile acids in the luminal side of the GI. Bile acid deconjugation has been implicated in several key transcriptional changes in circulation, liver and the GI tract. As bile acids deconjugate, hydrophobicity increases and cholesterol absorption is reduced, which results in better control of LDL-C levels in blood. Recent evidence shows that deconjugated bile acids are natural ligands of the farnesoid X receptor (FXR), a nuclear receptor present mainly in enterocytes and hepatocytes that plays an important role in the regulation of cholesterol uptake, metabolism, synthesis and efflux (Matsubara et al. 2012). In the intestines, this stimulation helps reduce lipid absorption. In the liver, FXR helps decrease bile acid uptake and stimulates elimination of bile acids and cholesterol by increasing expression of ATP-binding cassette (ABC) transporters from the liver to the gall bladder. Of note, mice colonized with active BSH bacteria resulted in significantly reduced weight gain, plasma cholesterol and liver triglycerides (Joyce et al. 2014). Taken together, increased bile acid deconjugation in the gut by commensal BSH can result in reduced cholesterol coming into the body and reduced circulating cholesterol in the blood.
**L. reuteri NCIMB 30242 is a Highly BSH-Active Probiotic and has been Extensively Characterized**

*L. reuteri* NCIMB 30242 was selected from a screening for BSH activity of over 100 strains, based on the aforementioned rationale. The strain has been named LRC™ and is currently deposited in the National Collection of Industrial and Food Bacteria international culture collection. *L. reuteri* NCIMB 30242 has been fully characterized both genotypically and phenotypically. The strain did not show any resistance to tested antibiotics with minimum inhibitory concentrations at or below the established guidelines of the European Food Safety Authority (EFSA). A careful analysis of the genomic sequence revealed no virulent genes, extra chromosomal DNA or mobile elements (Branton et al. 2010). In addition, the strain tested negative for production of the antimicrobial agent reuterin, as typically released by other *L. reuteri*. Furthermore, treatment of indicator microorganisms with *L. reuteri* NCIMB 30242 ferments did not result in growth inhibition, in contrast with ferments of positive controls, implying that the selected BSH-active strain is unlikely to produce the bacterial toxin bacteriocin. Finally no detectable release of biogenic amines such as histamine, tyramine, putrescine and cadaverine was observed in growth media fermented by *L. reuteri* NCIMB 30242.

An evaluation of the resistance of *L. reuteri* NCIMB 30242 to biological fluids was performed to help functionally characterize the strain. *L. reuteri* NCIMB 30242 showed superior resistance, as compared to commercial reference strains, when exposed to biological processes, including human and simulated gastric juice, simulated pancreatic secretion and human bile. Further, the long-term stability and suitability of *L. reuteri* NCIMB 30242 was confirmed in various commercial environments (Roy et al. 2016).

Safety of *L. reuteri* NCIMB 30242 was evaluated in vivo in rats and hamsters over a period of up to 8 weeks. No changes were observed in weight, animal activity, hematological parameters and serum chemistry markers (unpublished observations). Finally, histological analysis of tissues from major organs collected at necropsy at the end of these studies showed no pathologies.

**Clinical efficacy of L. reuteri NCIMB 30242 in cholesterol lowering**

*L. reuteri* NCIMB 30242 was tested for clinical efficacy to lower cholesterol in 2 independent randomized double-blind, placebo-controlled, multi-center clinical trials. In the first study, microencapsulated *L. reuteri* NCIMB 30242 was tested in a yogurt formulation (Jones et al. 2012a). The study included an intention-to-treat population of 114 hypercholesterolemic, otherwise healthy male and female subjects. The placebo group (58 subjects) and treatment group (56 subjects) received yogurt alone or a dose of not less than 1.4×10⁸ CFU of the microencapsulated test strain in yogurt, respectively, twice daily for the 6 week treatment period. General dietary recommendations were provided to the study subjects according to Canada’s Food Guide, Health Canada. The included subjects presented baseline serum LDL-C levels above 3.4 mmol/L and serum triglycerides (TG) levels below 4.0 mmol/L. No significant differences in serum lipids (total cholesterol (TC), HDL-C, LDL-C, TG, apoB-100, and non-HDL-C) were observed at baseline between placebo and treatment groups. Dietary assessment (total energy and composition of food intake) at baseline and endpoint revealed no differences between treatment groups. After the 6-week intervention, the *L. reuteri* NCIMB 30242 treated group presented a significant decrease in serum LDL-C levels of 8.92% (P=0.016) relative to the placebo group (Figure 1). Additionally, the *L. reuteri* treatment group showed significant reductions in serum TC of 4.81% (P=0.031) and non-HDL-C of 6.01% (P=0.029) as well as a tendency to reduce apoB-100 of 6.81% (P=0.092) over placebo (Figure 1). In contrast, TG and HDL-C remained unchanged over the course of the study.

The second study included an intention-to-treat population of 127 hypercholesterolemic, otherwise healthy male and female subjects randomized in a treatment group (66 subjects) or a placebo group (61 subjects) that received either not less than 2.9×10⁸ CFU of encapsulated *L. reuteri* NCIMB 30242 or control capsules with excipients only, respectively, twice daily for the 9-week course of the study (Jones et al. 2012b). Dietary recommendations were provided to the selected subjects and dietary assessment, performed as in the earlier study at baseline and endpoint reported no differences between experimental groups. Significant reductions in lipid levels in the *L. reuteri* group were observed after 6 weeks of treatment as compared to placebo controls and the changes were maintained by the end of the intervention. At the 9-week endpoint LDL-C in the *L. reuteri* NCIMB 30242 was reduced by 11.64% (P=0.001) over placebo (Figure 2). Also at endpoint, TC, non-HDL-C, and apoB-100 were reduced by 9.14% (P<0.001), 11.30% (P<0.001), and 8.41% (P=0.002), respectively over placebo (Figure 2). Neither TG nor HDL-C presented any significant differences over the course of the study in either experimental group. Markers for cardiovascular risk such as lipid ratios of LDL-C/HDL-C and apoB-100/apoA-1 were reduced by 13.39% and 9.00%, respectively in the *L. reuteri* supplement group over placebo controls. Other serum indicators for cardiovascular risk such as fibrinogen and hs-CRP showed significant reductions in the *L. reuteri* group as compared to placebo, over the duration of the trial. Fibrinogen was significantly
decreased by 14.25% in the treatment group over placebo. Further, hs-CRP presented significantly greater decreases from baseline to endpoint in the *L. reuteri* group as compared to placebo. In addition, based on the hs-CRP changes over the course of the study, 27% of the subjects receiving *L. reuteri* capsules reduced their relative risk category by one or more risk groups as compared with 1.7% of the subjects receiving placebo.

The cholesterol lowering efficacy of BSH-active *L. reuteri* NCIMB 30242 compares favorably with other recommended therapeutic dietary options for lowering LDL-C. Adding ~ 200 mg/day of *L. reuteri* NCIMB 30242 to the diet has been shown to reduce LDL-C by 9-12%, which is similar to LDL-C reductions observed with 2 g/day of phytosterols (AbuMweis et al. 2008, Demonty et al. 2009) and is more effective than 5-10 g/day viscous fibers (Anderson et al. 2000) or 25 g/day soy protein (Anderson et al. 2011).

Besides proven efficacy of *L. reuteri* NCIMB 30242 in cholesterol lowering and reduction in cardiovascular risk factors, the latter trial presented relevant data that supported the proposed mechanism of action. Total serum deconjugated bile acids augmented significantly in the *L. reuteri* NCIMB 30242 group, as compared to placebo over the intervention period. Cholesterol absorption was assessed by measures of serum plant sterols as surrogate markers. Mean concentrations of campesterol, sitosterol, stigmasterol and total plant sterols in the *L. reuteri* group were decreased by 41.5%, 34.2%, 40.7% and 38.9%, respectively, from baseline to endpoint relative to placebo. Finally, a significant association between bile acid deconjugation and cholesterol reduction was observed in subjects treated with *L. reuteri* capsules, whereas no association was detected in the placebo group.

While *L. reuteri* NCIMB 30242 has been shown to increase intraluminal bile acid deconjugation and as a result, increase deconjugated bile acids in plasma (Jones et al. 2012b), no change in fecal deconjugated bile acids has been observed (Jones et al. 2012a). It is postulated that bile acid deconjugation proximal to the terminal ileum alters the circulating bile acid pool, but does not lead to significant increases in fecal bile excretion in humans. In fact, intestinal bile acid transporters provide a highly efficient mechanism whereby the human intestinal tract can recover bile acids to the enterohepatic recirculation (Schiff et al. 1972, Dawson et al. 2011). Thus, evidence supports that *L. reuteri* NCIMB 30242 acts to deconjugate bile acids intraluminally and proximal to the colon and that deconjugated bile acids are efficiently re-absorbed.

In a follow-up pilot clinical study, BSH-active *L. reuteri* NCIMB 30242 was further assessed to understand its effect on bile acid response (Martoni et al. 2015). The primary outcome measure for this study was the change in plasma bile acid profile over the intervention period. Additional outcomes included circulating fibroblast growth factor (FGF)-19, plant sterols and LDL-C as well as strain-specific bsh gene presence in feces. Significant modulation of plasma bile acid profile was observed within one week of *L. reuteri* administration in delayed release capsules, indicating a rapid response that was subsequently maintained over the 4-week intervention period. Changes in bile acid profile were shown to be generally correlated with FGF-19 and inversely correlated with markers of sterol absorption. Additionally, fecal recovery of bile salt hydrolase gene copies specific to *L. reuteri* NCIMB 30242 was demonstrated in all treated subjects.

---

**PKAED WITH BENEFITS**: LRC™ is clinically proven to supply a host of health benefits.

### Dietary Cholesterol Management Options

| Table: Effective dose and cholesterol reduction of nutritional ingredients |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                | **EFFECTIVE** | **TC REDUCTION** | **LDL-C REDUCTION** | **EFFECT ON CV INFLAMMATORY MARKERS** | **INCREASE IN SERUM 25(HYDROXY)-VITAMIN D** | **EFFECT ON GI/HEALTH** |
|                                | **DOSE (g/DAY)** | **VS. PLACEBO (%)** | **VS. PLACEBO (%)** | **ON HDL/LDL RATIO** | **VS. PLACEBO (%)** | **REFERENCE** |
| LRC™ (L. reuteri NCIMB 30242)  | 0.2            | 5 – 9            | 9 – 12          | Yes              | Yes            | 22.4          | Yes | Jones et al., 2013; Jones et al., 2012a, Jones et al., 2012b; Ooi et al., 2010 |
| Phytosterols                   | 1.6 – 3        | 3 – 15           | 5 – 15          | Yes              | No             | 0             | No  | AbuMweis et al., 2008; Ortega et al., 2008; Takahashi et al., 2010; FDA, 2010; EFSA 2012 |
| Fish oil/ Omega-3/ DHA/EPA     | 0.85 – 3.4     | 0               | 0 – +3          | Yes              | Yes            | 0             | No  | Hooper et al., 2004; Skulas-Ray et al., 2011; EFSA, 2012 |
| Oat β-glucan                   | 3 – 10         | 4 – 9            | 5 – 10          | Yes              | No             | 0             | Yes | Oommen et al., 2011; Tappolet and Cummins, 2011; EFSA, 2010; EFSA, 2011; NCEP-ATP III, 2002 |
| Psyllium fiber                 | 7 – 10         | 2 – 9            | 3 – 7           | Yes              | No             | 0             | Yes | Wei et al., 2009; Anderson et al., 2009; NCEP-ATP III, 2002 |
| Soy protein                    | 25 – 40        | 3 – 5            | 4 – 6           | Yes              | No             | 0             | Yes | McGavig et al., 2006; Anderson and Bush, 2011; FDA, 1999; Enzman, 2006; NCEP-ATP III, 2002 |

* Effective dose in grams of dry ingredient
Clinical safety of *L. reuteri* NCIMB 30242

Clinical safety of *L. reuteri* NCIMB 30242 was thoroughly evaluated in the above randomized controlled trials (Jones et al. 2012c, Jones et al. 2012d). No serious adverse events were reported in either test group during the course of these studies. Additionally, no effects in weight, body mass index (BMI), systolic and diastolic blood pressure, heart rate or oral temperature were observed. Hematological parameters (RBC, WBC, hematocrit, hemoglobin, and platelets) showed no changes over the duration of the studies and no clinical significance was observed in the changes of blood chemistry parameters (urea, ALT, AST, GGT, alkaline phosphatase, bilirubin, creatinine, lipase, glucose, calcium, potassium, sodium, and chloride) before and after at least 9 weeks of treatment.

Additional clinical efficacy of *L. reuteri* NCIMB 30242

Among additional benefits, BSH-active *L. reuteri* NCIMB 30242 was shown clinically to significantly increase serum 25-hydrovitamin D (25(OH)D), the established indicator of vitamin D status (Jones et al. 2013a). Low serum 25(OH)D is common in the general population and has been associated with a range of ailments, including osteoporosis, cardiovascular disease and type II diabetes. In a post-hoc analysis of a randomized controlled clinical trial (Jones et al. 2013a), serum 25(OH)D, vitamin A, vitamin E, and β-carotene were assessed before and after a 9-week intervention period. The *L. reuteri* NCIMB 30242 group increased 25(OH)D by 14.9 nmol/l or 25.5% over the intervention period, which was a significant mean change relative to placebo of 17.1 nmol/l or 22.4% respectively (P=0.003). The significance of increased serum 25(OH)D in subjects consuming *L. reuteri* NCIMB 30242 capsules was also observed after adjustment for seasonality of the intervention period (P=0.001). Upon administration of *L. reuteri* NCIMB 30242, a significant association was observed between increases in serum 25(OH)D and decreases in the inflammatory marker hs-CRP (r = -0.208, P=0.023). No differences were observed in dietary intake or in circulating vitamin A, vitamin E or β-carotene.

*L. reuteri* NCIMB 30242 was similarly shown to be effective in supporting gastrointestinal (GI) health based on clinical Rome III questionnaire response (Jones et al. 2013b). Subjects were asked to complete a self-administered GI questionnaire in the day prior to the baseline (Week 0) and endpoint (Week 9) visits of the clinical study. These questions evaluated the severity or frequency of gastrointestinal symptoms and the responses consisted of a numeric value ranging from 0 to 6. The selected questions were grouped in four categories: burning, discomfort, constipation, and diarrhea. A GI health status score for each category was created by summing the numeric responses to the corresponding questions. Results indicated a significant improvement in general GI health status in subjects receiving *L. reuteri* as compared to placebo over the intervention period (P=0.029). Further, there was a significant improvement in diarrhea symptoms (P=0.018). No significant changes were observed between groups in symptoms related to burning, constipation or discomfort, although the latter two categories showed a tendency to amelioration in the *L. reuteri* treated group as compared to placebo (P=0.13 and 0.15, respectively).

Regulatory status of *L. reuteri* NCIMB 30242

Numerous unqualified strains of *L. reuteri* have a long-history of safe use in the food industry as a fermentation culture for the production of sourdough breads. Various strains of *L. reuteri* also have a history of safe use in food and supplement probiotic products. *L. reuteri* NCIMB 30242 (LRC™) has been issued a product license by Health Canada’s Natural and Non-prescription Health Products Directorate (NNHPD) based on its LDL and total cholesterol lowering properties. Products with a license have been assessed by Health Canada and found to be safe, effective and of high quality under their recommended conditions of use. It is identifiable by its Natural Product Number (NPN 80038469). Furthermore, LRC™ has self-affirmed Generally Recognized as Safe (GRAS) designation in the United States (U.S. Food and Drug Administration) and full GRAS notification has been submitted to the FDA (GRN No. 440, No NDl is required).

In the European Union, the *L. reuteri* probiotic species has Qualified Presumption of Safety (QPS) status. This assessment process recognizes that many microorganisms have long-histories of safe use by the food industry, and is based on four essential pillars of information: established identity, body of knowledge, possible pathogenicity, and end use. Following a review of the current uses of *L. reuteri* in food and feed products, the European Food Safety Authority (EFSA) concluded that the current food and feed uses of *L. reuteri* do not present cause for safety concern, and QPS status was granted for the species (EFSA J 2007). In Australia, the *L. reuteri* probiotic species is on the Therapeutic Goods Administration’s (TGA) approved list of medical ingredients (Therapeutic Goods Administration 2007). Lastly, the *L. reuteri* probiotic species is listed in the *Inventory of Microorganisms With Documented History of Use in Human Food* (Mogensen et al. 2002) as well as the list of Microorganisms with Technological Beneficial Use (Bourdichon et al. 2012).
Conclusion

Based on growing evidence on the role of bile acids in lipid metabolism and cardiovascular health, we selected and optimized *Lactobacillus reuteri* NCIMB 30242 for its high BSH activity. *L. reuteri* NCIMB 30242 presented clinical efficacy in cholesterol lowering, as well as safety and tolerability, in 2 well-powered, randomized, double-blind, placebo-controlled, multi-center clinical studies. The mechanism of action was evaluated by correlating the individual changes in deconjugated bile acids with changes in LDL-C to show that intraluminal BSH activity is responsible for the cholesterol lowering effect. Also, serum plant sterols, surrogate markers for cholesterol absorption, were found to decrease significantly as a result of treatment, suggesting inhibition of intestinal cholesterol absorption as a mechanism. A subsequent pilot study showed the potential of BSH-active *L. reuteri* NCIMB 30242 to significantly influence bile acid profile, FGF-19 and sterol absorption while improving LDL-C. Supplementation with BSH-active *L. reuteri* NCIMB 30242 has also been shown to ameliorate vitamin D status while supporting GI health. These results showcase the multi-faceted nature of this probiotic and provide a great opportunity to continue exploring its clinical benefits.
References

Figures

Figure 1. % change from baseline in total cholesterol (TC), apolipoprotein B-100 (apoB-100), non-HDL-cholesterol (non-HDL-C) and LDL-cholesterol (LDL-C) in subjects receiving a microencapsulated L. reuteri NCIMB 30242 yogurt formulation twice daily for 3 and 6 weeks as compared to placebo. *P<0.05; **P<0.01; ***P<0.001.

Figure 2. % change from baseline in total cholesterol (TC), apolipoprotein B-100 (apoB-100), non-HDL-cholesterol (non-HDL-C) and LDL-cholesterol (LDL-C) in subjects receiving a L. reuteri NCIMB 30242 capsule formulation twice daily for 3, 6 and 9 weeks as compared to placebo. *P<0.05; **P<0.01; ***P<0.001.
UAS Labs: The Probiotic Company

Founded in 1979, UAS Labs LLC has delivered the highest quality, science-backed probiotics to the natural products marketplace for more than 30 years. Strictly dedicated to probiotic manufacturing, UAS is committed to designing innovative and effective formulations including strains such as *L. acidophilus* DDS®-1. UAS products are sold to natural products retailers, health professionals, and private label customers and as ingredients to manufacturers in the U.S., Canada and over 55 other countries. The company is fully integrated from formulation through manufacturing, packaging and marketing, and adheres to the highest quality standards.

Our team has over 60 years of probiotic management experience and is driven to create unique, scientifically backed and stable products for any application. The team consists of highly educated scientists; Pharmacologists, Food Scientists, a Biochemist, a Medical Doctor, Microbiologists, Clinical Dietician/Nutritionist.

**THE UAS EXPERIENCE:** With over 60 years of probiotic management experience, our team has the knowledge and expertise to answer all of your probiotic needs.

*Probiotic Lactobacillus reuteri NCIMB 30242 (LRC™) for Heart Health Benefits*