

# Putting Science First: The International Scientific Association for Probiotics and Prebiotics (ISAPP)

Gregor Reid, BSc Hons, PhD, MBA, ARM, CCM, Dr Hs, FCAHS

The major reason for the formation of the International Scientific Association for Probiotics and Prebiotics (ISAPP) was to provide a “home” society for scientists working in different areas but commonly interested in microbiota, probiotics, and prebiotics. Since then, there has been a desire to clearly communicate the strengths of the science in these areas and to counter adverse perspectives. Created as a not-for-profit organization with a formal board, an industry advisory committee, and a students and fellows association, ISAPP has become the leading conduit for researchers in probiotic and prebiotic areas. Using mostly an invitation-only format with few oral presentations and an emphasis on working groups, ISAPP meetings have produced excellent contributions to the peer-reviewed literature, forged concepts that have been translated into new studies or regulatory frameworks, and created networks around the world. Through linkages with other organizations, ISAPP will continue to reach out to every continent to inspire others to move this important field forward.

**Key words:** *Probiotics, prebiotics, science*

## Emerging from Snake Oil Wagons

By 2000, I had been working for 18 years on the use of probiotics for urogenital health. A growing number of other scientists had also been studying the probiotic effects of microbes, mostly in relation to gastrointestinal applications. However, an all-too-large number of people remained skeptical about the idea that microbes could provide health benefits. Often the term *probiotic* was spoken of as “snake oil,” in reference to products sold off the back of wagons in the early days of America’s wild west. The epitome of this opinion was expressed rather strikingly in 1999 by Dr. Ron Atlas, president of the American Society for Microbiology: “Probiotics may be today’s snake oil, the liquid concoction of dubious or worthless medical value fraudulently peddled by hawkers from the backs of covered wagons during the settlement of the United States as a cure for innumerable ills.”<sup>1</sup> As one of the “hawkers” who had never been on the back of a covered wagon, was quite scared of snakes, and did not sell

any medical concoction, I was sorry that this perception could come from the head of such a respected organization.

Although not in any way influenced by Atlas’s comments, scientists working in the areas of probiotics and their younger cousins, prebiotics, were aware that the scientific credibility of these areas was low. There was no universally accepted definition for probiotics, a number of products on the market were of dubious quality and unproven efficacy, and the concept that a food or supplement could be beneficial seemed a distant reality. On the other hand, some excellent products were available, especially in Asia and Europe, with outstanding science supporting their effects. In May 2000, at a Fermented Foods and Health Meeting in New York City, a small group of scientists led by Dr. Mary Ellen Sanders and Dr. Glenn Gibson met to discuss the formation of a multi-disciplinary scientific organization dedicated to specifically addressing the dynamic, fast-moving, and increasingly popular fields of probiotics and prebiotics. No similar organization specifically dedicated to probiotics and prebiotics existed. The enthusiasm for such an organization was strong, and word soon spread about the concept. Dr. Sanders had an excellent reputation as a scientist and industry consultant, and Dr. Gibson was an international leader in prebiotics, having created the definition with Marcel Roberfroid in 1995: “A prebiotic is a nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one

Gregor Reid: *Department of Microbiology and Immunology, The University of Western Ontario, and Canadian R&D Centre for Probiotics, Lawson Health Research Institute, London, ON.*

Reprint requests: Dr. Gregor Reid, *Canadian R&D Centre for Probiotics, F2-116, Lawson Health Research Institute, 268 Grosvenor Street, London, ON N6A 4V2; e-mail: gregor@uwo.ca.*

DOI 10.2310/6180.2010.00017

© 2010 Decker Publishing

**DECKER**<sub>X</sub>

or a limited number of bacteria in the colon, and thus improves host health.”<sup>2</sup>

In May 2002, I hosted an open forum and the first meeting of the International Scientific Association for Probiotics and Prebiotics (ISAPP) in London, Ontario. The format was different from that of most other conferences in that it emphasized group discussions on specific issues and welcomed input from companies that were committed to research and development activities in the field. The event was a great success, with 63 scientists attending, a peer-reviewed publication emerging from it,<sup>3</sup> and friendships seeded by outdoor activities in the blazing sunshine, the most notable being Bob Rastall winning a large teddy bear in a tree hunt. The ISAPP was formally established in August 2002 as a nonprofit, tax-exempt 501(c)(3) corporation in California. To manage the administrative affairs of ISAPP, we contracted the California Dairy Research Foundation (CDRF), in Davis, California, which, in addition to philosophical support of the objectives of ISAPP, provided administrative support through its offices. The ISAPP mission statement is “to engender and disseminate information on high quality, multidisciplinary, scientific investigation in the fields of probiotics and prebiotics, and to advance the development of scientifically substantiated, health-promoting probiotic and prebiotic products worldwide.”

The founding Board comprised Mary Ellen Sanders as president, Glenn Gibson as vice president, myself as secretary, and Harsharn Gill as treasurer, accompanied by Todd Klaenhammer, Ian Rowland, Bob Rastall, Marcel Roberfroid, Christine Cherbut, David Mills, and Joseph O'Donnell. As we had organized an international event, the next main task was to establish policies and procedures. There was unanimous belief that ISAPP should be an organization partnering with industry but completely independent and not for profit.

### **Setting Up the ISAPP's Structure and Primary Goals**

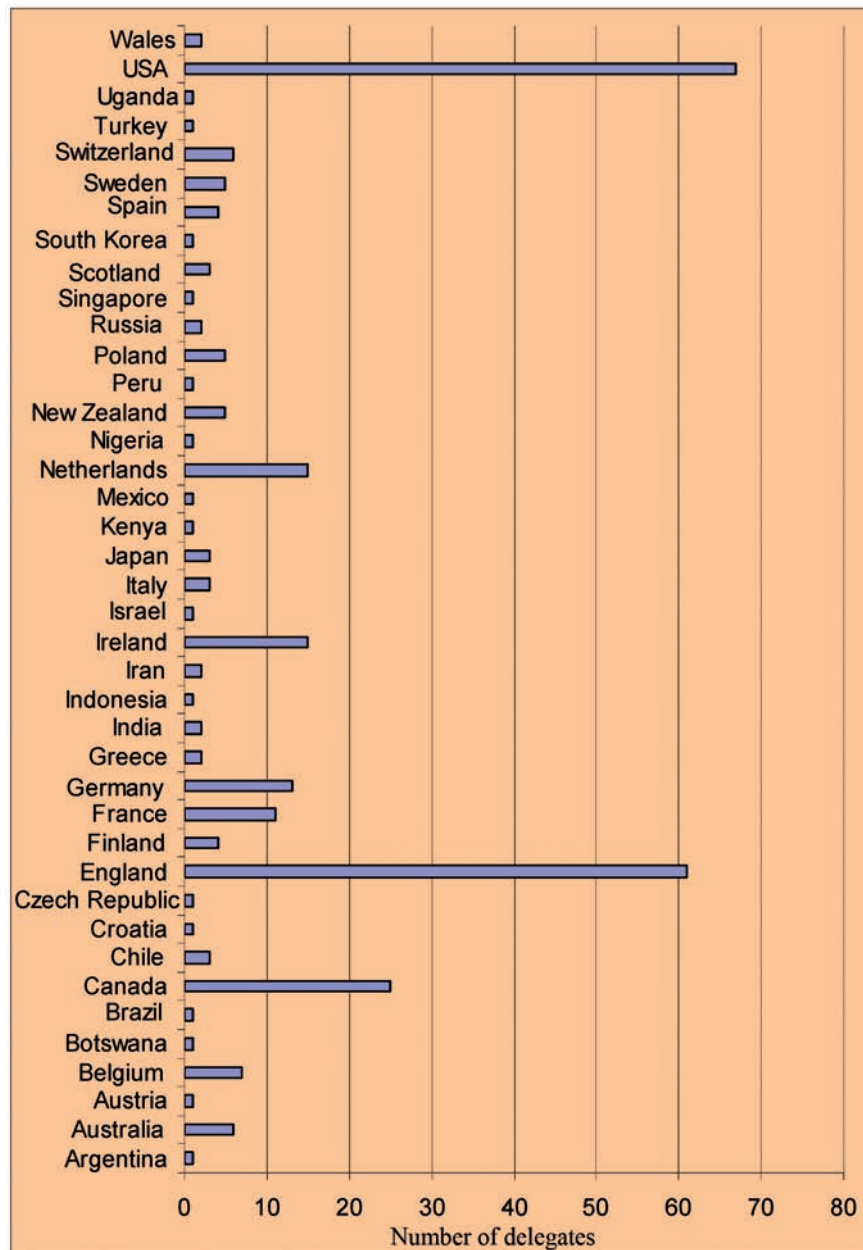
In addition to Mary Ellen Sanders, two people deserve recognition for helping ISAPP get off the ground. Irene Lenoir-Wijnkoop from Danone stepped forward at the initial New York meeting and provided a significant research grant as well as logistical support. This was remarkable given that Danone was aware that ISAPP would be neutral in terms of industry sponsorship. Indeed, companies including competitors of Danone, such as Nestlé, soon followed with financial assistance. The second advocate was Joseph O'Donnell, executive director of the CDRF. In due course, the CDRF helped

with logistics, financial management, and the creation of our constitution.

A decision was made early on in ISAPP's evolution not to have formal membership. The Board members were all volunteers with busy academic careers, and with industry sponsorship through annual fees, it was decided that there was no need to acquire dues from individuals. Tracking down dues and providing members with something for their dues (a newsletter, a journal, an annual conference, travel grants, or whatever) was viewed as being too laborious. Furthermore, the Board decided that each conference workshop should examine topical themes and invite appropriate participants. Thus, some people who were ideal conference participants one year may not have been the next year if topics were outside their expertise. Such a decision would not go down well if ISAPP had members as they would expect to be free to attend every conference. This decision was not easy to make, and the Board rediscusses this almost annually. Ultimately, there are insufficient funds to invite all the people we feel can contribute to every meeting. Still, since ISAPP's inception, over 300 delegates have attended the main annual ISAPP events from 40 countries (Figure 1), something that we feel is a major accomplishment. Given the critical mass of science being done in North America and Europe and the location of Industry Advisory Committee (IAC) members, the majority of participants have come from countries in which ISAPP meetings have been held. Nevertheless, efforts are ongoing to globalize the outreach of the organization, and, to date, we have supported symposia in Argentina, Canada, India, Indonesia, Poland, Russia, South Africa, and the United States, thereby reaching many other scientists, health care professionals, and laypeople around the world.

The outstanding support from industry that enabled the first workshop to be held, and the belief of all the Board members that industry is a natural extension of science, making it possible for new products to emerge from the bench and be tested in our clinics, led to the establishment of an IAC. Permitted to have up to two science-oriented representatives at an ISAPP event, each industry partner has an equal place on the IAC, and, collectively, they vote for two delegates to represent the IAC on the ISAPP Board. IAC companies should have the following:

- A science-based approach to probiotic and prebiotic product development
- A commitment to, and funding of, related research



**Figure 1.** Over 300 scientists from 40 countries have attended International Scientific Association for Probiotics and Prebiotics (ISAPP) annual meetings. Industry scientists and attendees at events cosponsored by ISAPP in Argentina, Canada, India, Indonesia, Poland, Russia, South Africa, and the United States, not listed here, bring the numbers to over 1,000 people.

- A commitment to responsible product formulation and communications
- A commitment to the mission of the ISAPP and a willingness to work toward that mission in a collaborative manner with ISAPP Board of Directors and other IAC members
- Willingness to pay established IAC membership fees and take an active role in the IAC

This unique relationship with industry is a backbone accomplishment of the ISAPP.

Thomas Tompkins, director of research at Lallemand, chaired the first IAC meeting in 2003. In 2008, the Board asked the IAC to name a representative as a nonvoting member of the Board, to chair IAC meetings, and to convey to the Board the views and suggestions from the IAC. To this day, the proactive and responsive IAC has

provided excellent feedback to the Board. In 2009, 25 of the world's leading research and development companies in probiotics and prebiotics were represented on the IAC.

### ISAPP's Contributions to the Field of Functional Foods

There are several ways in which an organization's contribution to a particular field can be measured, depending on who asks the question and with what perspective. At least five stakeholders might benefit from ISAPP: (1) scientists (and students and fellows interested in pursuing these areas as a career path) who study human or animal and bacterial nutrients and microbes that are either probiotic or part of the host microbiome; (2) clinicians and other professionals, such as dietitians, nurses, and nutritionists, who are interested in new ways to manage patient care, sometimes in very challenging settings in the developing world; (3) companies interested in the production and distribution of probiotics and prebiotics; (4) the media who report on various aspects of probiotics and prebiotics from science to business and consumer issues and laypeople either taking these products or wanting to learn more about which ones work and how; and (5) governments wanting to understand how best to regulate these products. The ISAPP has held workshops of interest to all of these stakeholders and tried to provide outcomes that contribute information that is current and pertinent.

For scientists, key issues include which strains would make an effective probiotic, how they confer their benefits and which organisms are influenced most by prebiotic applications. Discussing such topics invariably captures a wide array of scientific areas, from engineering strains, to express human immunodeficiency virus (HIV)-inhibitory molecules and antiinflammatory mediators, to programming the gut microbiota in newborns, modulating immunity and the microbial ecology of the gut, and reducing the risk of cancer and other diseases, as discussed at meetings in the United States, Northern Ireland, and Canada.<sup>4-8</sup>

Clinicians, surgeons, and allied medical professionals benefit from insight into good clinical trial design, clinical end points, probiotic safety, and how studies can increase the number of subjects responding to interventions. ISAPP workshops have discussed these issues and review articles have been duly published,<sup>9-12</sup> and provided unmatched opportunities for building research collaborations that facilitated new projects. In addition, ISAPP commissioned an article on a topic of interest to pediatricians, namely

whether D-lactate-producing probiotic strains are safe for infants.<sup>13</sup> In an open-forum format in London, United Kingdom, the important topic of how to deliver probiotics to poor, malnourished rural people was discussed.<sup>14</sup> The fact that so few scientists or clinicians were working on this topic made it difficult to gain a comprehensive grasp of the challenges. This situation emphasizes the need for information from ISAPP meetings to be shared globally, and encourages scientific programs to be established in more countries.

For industry, there are several needs. The reputation of the area is critical for credibility and explaining how products work. Attending companies gain first hand access to many experts and the latest data emanating from global laboratories. The ability of an independent body such as ISAPP to counter criticisms made in the public or scientific domain is also very important.

As a nonprofit organization, ISAPP is legally precluded from lobbying or otherwise influencing the legislative process, but its scientists provide a neutral voice that may speak without the appearance of conflict of interest. Input from ISAPP can simply take the form of validating the studies produced by industry or on marketed products. It can also be a guide through informative presentations to regulatory agencies in dealing with probiotics and prebiotics. In addition, ISAPP can attempt to counter comments made in the press or even conclusions drawn about a scientific study or a strain. For example, ISAPP or its members published critical rebuttals of the use of the name *Lactobacillus sporogenes* as a probiotic<sup>15</sup> or the suggestion that "dead probiotics" exist,<sup>16,17</sup> that probiotics cause obesity,<sup>18</sup> or that genetically engineered strains are, by necessity, dangerous and should be banned,<sup>19</sup> and countered inflammatory statements made in the report of an ill-conceived clinical study that resulted in the death of some study subjects.<sup>20</sup>

In a break from the tradition of most scientific conferences, ISAPP held a workshop with media representatives in 2008 to explore the challenges faced by acquiring, evaluating, and reporting news about probiotics and prebiotics. It is clear that many factors influence what news gets out, how, why, and to whom. Staff cutbacks in traditional media mean that fewer qualified science writers are available to cover this topic; therefore, it is helpful to reporters if scientists describe their work in very simple language.<sup>21</sup> Web-based blogs, Internet sites, and Facebook now provide ways to disseminate information, but in most cases, the content is not peer reviewed and can appear out of context, inaccurate, or misleading. Some people might argue that Andy Warhol's 15 minutes of fame concept

stands up and that any publicity is good publicity. I disagree. There are too many incorrect statements being made on the Web, at conferences, and in the media that show that the term *probiotic* is not understood, despite several publications clarifying the definition and what it means ([http://www.isapp.net/pp\\_intro.asp](http://www.isapp.net/pp_intro.asp)). ISAPP Board members actively speak with the media and clarify these issues, and it is hoped that, in time, there will be a realization that scientific evidence is necessary before naming a product probiotic, prebiotic, or synbiotic (a combination of prebiotics and probiotics).

Finally, as with other functional foods, probiotics and prebiotics need to be regulated. This presents many issues that ISAPP has grappled with since its inception.<sup>22</sup> Including Japan, where legislation has long been in place, there is no universally accepted way of handling the regulations. In particular, in recent times, ISAPP has led discussions on major issues emanating from how the European Food Safety Authority, the Food and Drug Administration of the United States, and Health Canada have been approaching regulation of probiotic and prebiotic products. The latter, through the Natural Health Products Directorate, has instigated a product monograph intended to serve as a guide to industry for the preparation of Product Licence Applications for natural health product market authorization of probiotics ([http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licen-prod/monograph/mono\\_probioti-eng.php](http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licen-prod/monograph/mono_probioti-eng.php)). There are intense feelings about these issues, especially as they can advance or retract the business interests of many companies and limit or permit the use of products in clinical trials run by ISAPP scientists. Whatever the outcome, it is hoped that all regulatory processes will honor the appropriate use of the terms *probiotics* and *prebiotics* so that consumers are as informed as possible about the degree of documentation for each product, irrespective of the claims (whether approved or not) made on the labels. ISAPP will certainly promote colloquial discussion on these important regulatory topics.

### The Future for the ISAPP

The November 2009 meeting following the National Academy of Sciences Sackler Colloquium in Irvine, California, was in some ways a turning point for the next phase of the organization. The impact of metagenomics, transcriptomics, metabolomics, and other such “omic” research is clearly starting to revolutionize the field. New candidate probiotic strains will be discovered from the plethora of organisms being identified in the host. These

will include strains that are genetically modified. Identification of critical functions performed by indigenous microbes will lead to new compounds and formulations that improve health. Included in this will be new prebiotics that are metabolized by the microbiota in a manner that influences multiple host functions, locally and at distant sites. ISAPP’s role will be to continue to identify these advances at an early stage, challenge their usefulness, help link different disciplines, and bring them to the attention of other scientists and industry partners.

The Sackler Colloquium, and the ISAPP meeting that followed it in 2009, illustrated the expanding areas of the human body that are affected by beneficial microbes. Studies in the brain and central nervous system illustrate how influential some microbes can be on health and well-being, whereas the potential to “program” the fetus and newborn raises the question of how we deal with ethical and moral issues. Progress will inevitably attract pharmaceutical, biotechnology, diagnostic, consumer, and medical device companies to the field, and with them more financial power to tackle mechanistic questions. More and more clinicians are recommending probiotics or are interested in using them to manage disease, and their hands-on patient experience will expand our understanding of the efficacy and limitations of probiotic food.

The future of any organization lies in the strength of its successors. In 2009, ISAPP created the Students and Fellows Association (SFA) as a vehicle to capture and embrace the collective ideas and energy of young scientists working in areas associated with the ISAPP mandate. The objectives of the SFA are to facilitate the professional development of students and fellows doing research in the field of microbe-mediated health effects. To do so, the association will

1. Represent students and fellows to the ISAPP Board of Directors
2. Organize professional development training for its members
3. Obtain and offer grants to its members for professional development
4. Offer a platform for interaction between students, senior scientists, and industry

This exciting group of young professionals will be represented at each ISAPP meeting by a President and a Secretary plus others who participate in the discussion groups. Linking to other students and fellows around the world through Facebook and other social networking, the SFA will organize meetings, webinars, mentoring, and career sessions and exchange ideas and laboratory techniques and questions.

**Table 1.** ISAPP Board of Directors, 2009–2010

<i>Position</i>	<i>Name</i>	<i>Institute</i>
President	Glenn Gibson	University of Reading, Reading, England
Vice president	Todd Klaenhammer	North Carolina State University, Raleigh, CA, USA
Treasurer	Karen Scott	Rowett Research Institute, Aberdeen, Scotland
Secretary	Michael Cabana	University of California, San Francisco, CA, USA
Past president	Gregor Reid	The University of Western Ontario, London, ON, Canada
Executive director	Mary Ellen Sanders	Dairy and Food Culture Technologies, Centennial, CO, USA
Member at large	Nathalie Delzenne	Université Catholique de Louvain, Brussels, Belgium
Member at large	George Fahey	University of Illinois, Urbana-Champaign, IL, USA
Member at large	Colin Hill	University College Cork, Cork, Ireland
Program chair	Francisco Guarner	University Hospital Vall d'Hebron, Barcelona, Spain
Industry Advisory Committee	Duane Charbonneau	Procter & Gamble, Mason, OH, USA
President, Students and Fellows Association	Delphine Saulnier	Baylor College of Medicine, Houston, TX, USA

ISAPP = International Scientific Association for Probiotics and Prebiotics. More details are available at <<http://www.isapp.net>>.

Since ISAPP's inception, other probiotic organizations have emerged, and many conferences have been, and will be, held on the topic. Indeed, some might suggest that there are now too many venues for discussion of probiotics and prebiotics. The ISAPP's workshop format still remains quite unique, even from Keystone and Gordon conferences. The current Board (Table 1) is committed to continuing the organization's outreach to various countries through partnering. This is an important part of ISAPP's evolution and should continue in the future, not just as markets open up for probiotic and prebiotic products but perhaps more so because too many people who can benefit are not receiving these therapeutics. Likewise, education programs need to continue to reach caregivers and laypeople around the globe so as not to overly raise expectations of what these products can do, yet explaining that more attention needs to be paid to beneficial microbes and the maintenance of health.

### Acknowledgment

Financial disclosure of author: I declare that in 2008 I transferred patents and probiotic strains to Chr Hansen. The Lawson Health Research Institute received a donation from Danone, which it used to endow a research chair in human microbiology and probiotics, which I now hold, but I remain an independent academic scientist. I am not a salaried consultant for any probiotic or prebiotic company.

Financial disclosure of reviewers: None reported.

### References

1. Atlas RM. Probiotics—snake oil for the new millennium? *Environ Microbiol* 1999;1:377–82.
2. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *J Nutr* 1995;125:1401–12.
3. Reid G, Sanders ME, Gaskins HR, et al. New scientific paradigms for probiotics and prebiotics. *J Clin Gastroenterol* 2003;37:105–18.
4. Guarner F, Bourdet-Sicard R, Brandtzaeg P, et al. Mechanisms of disease: the hygiene hypothesis revisited. *Nat Clin Pract Gastroenterol Hepatol* 2006;3:275–84.
5. Lenoir-Wijnkoop I, Sanders ME, Van Loo J, et al. Probiotic and prebiotic influence beyond the intestinal tract. *Nutr Rev* 2007;65:469–89.
6. Rastall RA, Gibson GR, Gill HS, et al. Modulation of the microbial ecology of the human colon by probiotics, prebiotics and synbiotics to enhance human health: an overview of enabling science and potential applications. *FEMS Microbiol Ecol* 2005;52:145–52.
7. Reid G. Probiotics and prebiotics—progress and challenges. *Int Dairy J* 2008;18:969–75.
8. Sanders ME, Guarner F, Mills D, et al. Selected topics in probiotics and prebiotics: meeting report for the 2004 International Scientific Association for Probiotics and Prebiotics. *Curr Iss Intest Microbiol* 2005;6:55–68.
9. Reid G, Anukam K, James VI, et al. Oral probiotics for maternal and newborn health. *J Clin Gastroenterol* 2005;39:353–4.
10. Tompkins TA, Sanders ME. Good intentions, poor study design. *Can Fam Physician* 2004;50:1499–500.
11. Reid G, Gaudier E, Guarner F, et al. Responders and non-responders to probiotic interventions: how can we improve the odds? *Gut Microbes* 2010;1(3):200–204.
12. Sanders ME, Akkermans LMA, Haller D. Safety assessment of probiotics for human use. *Gut Microbes* 2010;1(3):164–185.
13. Mack D. D(–)-lactic acid producing probiotics, D(–)-lactic acidosis and infants. *Can J Gastroenterol* 2004;18:671–5.

14. Reid G, Anand S, Bingham MO, et al. Probiotics for the developing world. *J Clin Gastroenterol* 2005;39:485–8.
15. Sanders NE, Morelli L, Tompkins TA. Sporeformers as human probiotics: *Bacillus*, *Sporolattobacillus*, and *Brevibacillus*. *Comp Rev Food Sci Food Saf* 2003;2:101–10.
16. Reid G, Guarner F, Gibson G, et al. International Scientific Association for Probiotics and Prebiotics. Discussion on Toll-like receptor 9 signaling mediates the anti-inflammatory effects of probiotics in murine experimental colitis. *Gastroenterology* 2004; 127:366–7.
17. Sanders ME, Hamilton J, Reid G, Gibson G. A nonviable preparation of *Lactobacillus acidophilus* is not a probiotic. *Clin Infect Dis* 2007;44:886.
18. Delzenne N, Reid G. No causal link between obesity and probiotics. *Nat Rev Microbiol* 2009;7:901.
19. Reid G, Gibson GR, Gill HS, et al. Use of genetically modified microbes for human health. *Microbial Ecol Health Dis* 2006;18:75–6.
20. Reid G, Gibson G, Sanders ME, et al. International Scientific Association for Probiotics and Prebiotics. Probiotic prophylaxis in predicted severe acute pancreatitis. *Lancet* 2008;372:112–3.
21. Reid G. The media and probiotics: provocation or dialogue? *Int J Probiotics Prebiotics* 2010. [In press].
22. Sanders ME, Tompkins T, Heimbach J, Kolida S. Weight of evidence needed to substantiate a health effect for probiotics and prebiotics: scientific and regulatory considerations in Canada, EU, and U.S. *Eur J Nutr* 2005;44:303–10.