



## **2005 Annual Report**

### **International Scientific Association for Probiotics and Prebiotics**

January 1 – December 31, 2005

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#### **Introduction**

ISAPP is an international non-profit collaboration of scientists dedicated to advancing the science of probiotics and prebiotics. The mission statement of ISAPP 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. ISAPP is the only scientific organization dedicated specifically to probiotics and prebiotics, bringing together scientists from all pertinent disciplines, including food science, microbiology, immunology, biochemistry, nutrition, molecular biology and medicine. As a scientific society, ISAPP strives to have all activities focused on science, not the promotion of any specific commercial products.

For additional details, see website [www.isapp.net](http://www.isapp.net)

#### **Message from the President**

2005 represented a departure from ISAPP's normal approach to facilitating communication with the scientific community. Instead of sponsoring one meeting attended by invited delegates, the Board recommended that we attempt to expand our communication efforts to parts of the world not reached by past ISAPP events. The most efficient approach to this was to partner with other scientific organizations. Therefore, ISAPP sponsored symposia in Indonesia, Poland, South Africa and North America. Summaries prepared by ISAPP representatives to these meetings are in the appendices of this report. For the future, ISAPP will continue to support such satellite efforts, but will do so in addition to its own meeting, rather than in lieu of.

The probiotic and prebiotic fields continue to grow and develop, both scientifically and commercially. This is reflected by many worldwide activities. For just a hint of this activity, see projects like ACE-ART ([www.ace-art.net](http://www.ace-art.net)), an EU project on antibiotic resistance in bacteria belonging to genera used as probiotics; PROSAFE, PROTECH and SYNCAN, EU projects focused on biosafety, technological considerations and impact on cancer endpoints in humans, respectively - all pivotal research undertakings for this field; efforts by the European Food Safety Authority ([www.efsa.europa.eu](http://www.efsa.europa.eu)) to establish an approach for the safety assessment of



microorganisms deliberately added to food and feed; American Academy of Microbiology, which convened a colloquium in the U.S. to discuss the impact of probiotics on human microbial ecosystems and health; and the emergence of an organization in Holland “Gut Flora”, which conducted its first meeting on the topic of gut flora in health and disease in 2005 ([www.probiotic-amsterdam.org](http://www.probiotic-amsterdam.org)). These science-based efforts on the part of numerous parties bode well for the health of this field.

Once again, I find myself at year’s end ever grateful for the support and scientific guidance of the ISAPP Board of Directors and my many other supportive colleagues in industry and academia.

A handwritten signature in cursive script that reads "Mary Ellen Sanders".

**Signed: Mary Ellen Sanders**



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There were no changes from 2004 to the Board of Directors.

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## 2005 Accomplishments

- **ISAPP-sponsored symposia and meetings**

In 2005, the ISAPP Board of Directors decided to expand ISAPP's reach beyond its past presence in North America and Europe. Especially of interest was to expand scientific communication to regions of the world not easily able to participate in state-of-the-art conferences on probiotics and prebiotics. Toward this end, we are now pleased to report that we have helped set up or will be participating in conferences or mini-symposia in several locations:

- *Asia:*

3rd Asian Conference for Lactic Acid Bacteria & 9th National Congress of Indonesian Society for Microbiology, Indonesia August 24-27, 2005 held in Bali, Indonesia [www.aclab-3.ugm.ac.id](http://www.aclab-3.ugm.ac.id). For report, see Appendix A.

- *Eastern Europe:*

ISAPP sponsors EUROPEAN CONFERENCE ON PROBIOTICS AND THEIR APPLICATIONS <http://confer.uj.edu.pl/euprobio> Krakow 6 - 8 October 2005  
For report, see Appendix B.

- *Africa:*

18th International Nutrition Congress, Gastroenterology - Probiotics and beneficial impact on health, S. Africa, September 2005  
<http://www.puk.ac.za/fakulteite/voeding/iuns/>  
For report, see Appendix C.

- *North America:*

American Academy of Microbiology Colloquium, Probiotic Microbes: The Scientific Basis, November 2-5, 2005, Baltimore, Maryland, USA. For report, see Appendix D.

International Union of Microbiological Societies, symposium titled "Probiotic Functions of Microorganisms", July 27, 2005 San Francisco, California, USA. For report, see Appendix E.

- **Met with United States Pharmacopeia to discuss development of standards for probiotics**

Discussions regarding development of standards for probiotic products were convened by ISAPP. An ISAPP-sponsored meeting was held with scientists and managers at USP (United States Pharmacopeia [www.usp.org/](http://www.usp.org/); USP dietary supplement program [www.usp.org/USPVerified/dietarySupplements/](http://www.usp.org/USPVerified/dietarySupplements/)). USP is a non-profit organization (highly regarded by the FDA) which, along with industry, develops standards for active ingredients in drugs and dietary supplements. Currently, no standards exist for probiotics or prebiotics. They are interested in working with ISAPP and interested industry partners for developing standards for specific products. These standards would specify levels of active ingredients through the end of shelf life. The program and adherence to standards would be voluntary,



but products adhering to the standards would be able to display the USP symbol, a powerful communication tool for industry to consumers. This program would not entail validating claims of efficacy. USP has affiliates in Europe and Japan.

- **ISAPP publications to date**

- Reid G, Anand S, Bingham MO, Mbugua G, Wadstrom T, Fuller R, Anukam K Katsivo M. 2005. Probiotics for the developing world. *J Clin Gastroenterol.* 39(6):485-8.
- Anukam KC, Reid G. 2005. Providing probiotics to sub-Saharan Africa: ethical principles to consider. *J. Complem. Integrat. Med.* 2(1) [www.bepress.com/jcim/vol2/iss1/10/](http://www.bepress.com/jcim/vol2/iss1/10/).
- Rastall R, Gibson G, Gill H, Guarner F, Klaenhammer T, Pot B, Reid G, Rowland I, Sanders ME. 2005. 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 Microbial Ecology* 52(2): 145-152.
- Sanders ME, Tompkins T, Heimbach J, Kolida S. 2005. 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.* 44(5):303-10.
- Sanders ME, Guarner F, Mills D, Pot B, Rafter J, Rastall R, Reid G, Ringel Y, Rowland I, Saarela M, Tuohy K. 2005. Selected topics in probiotics and prebiotics: meeting report for the 2004 International Scientific Association for Probiotics and Prebiotics. *Cur Iss Intestinal Microbiol.* 6: 55-68.
- Sanders ME. 2005. Objectives and activities of the International Scientific Association for Probiotics and Prebiotics. In, Cesare Schiavi (Ed.) *Probiotics, Biotherapeutics & Health.* Mofin Alce, Novara, Italy., p. 206-216.
- Tompkins TA, Sanders ME. 2004. Good intentions, poor study design. *Can Fam Physician.* 50:1499-500.
- Mack D. 2004. D(-)-lactic acid producing probiotics, d(-)-lactic acidosis and infants. *Canadian J Gastroenterol.* 18:671-5.
- Reid G, Guarner F, Gibson G, Tompkins T, Gill H, Rowland I, Rastall B, Pot B, Sanders ME. 2004. Discussion on toll-like receptor 9 signaling mediates the anti-inflammatory effects of probiotics in murine experimental colitis. *Gastroenterology.* 127:366-7.
- Reid G., Sanders ME, Gaskins HR, Gibson GR, Mercenier A, Rastall R, Roberfroid M, Rowland I, Cherbut C, Klaenhammer T R. 2003. New scientific paradigms for probiotics and prebiotics. *J Clin Gastroenterol.* 37:105-118.
- Ferber D. 2002. Much ferment on the probiotics front. *ASM News.* 68:369-370.

- **Board of Directors Meeting**

- October 5 and 8, 2005, Amadeusz Hotel, Krakow Poland

## **2006 Objectives**

- 2006 Annual meeting at University of Ulster, Coleraine, Northern Ireland with Board member Ian Rowland as local host.
- Consider expanding our concept of meetings to include the development of small working group meetings to explore 'best approaches' for evaluation of efficacy for probiotics and prebiotics in specific areas of research. Initially, one key efficacy endpoints should be chosen (e.g., allergy). Then about 5 clinical researchers, 5 interested industry scientists, several ISAPP scientists (total maximum about 15 people) would meet for one day to



discuss best clinical approaches. If this pilot goes well, we would hope to convene groups with different targets, such as intestinal microbiology, wellness, etc.

- Collaborate with WHO/FAO to develop a Codex 'standard of identity' for the use of the term 'probiotic'. If adopted, products using this term on product labels would have to meet certain minimum criteria of safety, product composition and efficacy.



## **Appendix A. Report from ISAPP-sponsored meeting in Bali**

Report filed by Harsharn Gill, ISAPP Treasurer:

A satellite symposium on Probiotics and Prebiotics, sponsored by ISAPP, was held in conjunction with the 9th National Congress of Indonesian Society for Microbiology & 3<sup>rd</sup> Asian Conference for Lactic Acid Bacteria in Bali, Indonesia (25-26 August 2005). The conference was organized in collaboration with International Union of Microbiological Societies and the Asian Federation of Society for Lactic Acid Bacteria. Over 330 participants from 15 countries, including 5 from Europe, participated in the conference. The conference program consisted of 7 plenary papers, 54 oral presentations (12 satellite symposia) and 139 poster presentations. Two of the plenary speakers (Prof J Crane, Wellington School of Medicine and Health Sciences, New Zealand and Prof H Gill, DPI Victoria, Melbourne, Australia) and two of the symposium speakers (Dr R Crittenden, Food Science Australia, CSIRO, Melbourne, Australia and Dr J Prasad, Fonterra Innovation, Fonterra Co-operative Group Ltd, Palmerston North, New Zealand) were sponsored by ISAPP. Their talks were titled:

- Not all bacteria are bad: probiotics improve health and fight disease (Harsharn Gill)
- 30 years of the hygiene hypothesis (Julian Crane)
- Prebiotics, gut microbiota, and human health (Ross Crittenden)
- Probiotic and the manipulation of intestinal microflora in the elderly (Jaya Prasad)

All presentations were very well received and generated much discussion and interest in the area.



## Appendix B. Report from ISAPP-sponsored meeting in Poland

### EUROPEAN CONFERENCE ON PROBIOTICS AND THEIR APPLICATIONS

<http://confer.uj.edu.pl/euprobio>

Krakow 6 - 8 October 2005

**Report filed by Mary Ellen Sanders, ISAPP President (with input from Francisco Guarner, Gregor Reid, Bruno Pot, James Versalovic and Joseph Rafter):**

ISAPP was honored to be a sponsor of EUPROBIO meeting on probiotics held October 5-9, 2005 and organized by Dr. Piotr Heczko. Set in the beautiful city of Krakow in a brand new lecture hall on the Jagiellonian University, the meeting covered the topics of immunology, technological issues related to probiotic production, gastrointestinal diseases, *H. pylori*, global health applications, allergy, and vaginal applications. The speakers were from countries worldwide including South Africa, Canada, USA across Europe. ISAPP sponsored travel for Mary Ellen Sanders (USA), Gregor Reid (Canada), Francisco Guarner (Spain), Bruno Pot (Belgium) and James Versalovic (USA), each of whom chaired sessions and gave talks on their specific areas of expertise. In addition, Gregor Reid played a major role in the development of the scientific program. The meeting was attended by about 300 people.

Some observations from the meeting include:

- Many definitions of probiotics have been advanced and older versions continue to be quoted by a number of scientists. It is ISAPP's view that the FAO/WHO 2001 definition be adopted. If one accepts the FAO definition ([www.fao.org/es/ESN/Probio/probio.htm](http://www.fao.org/es/ESN/Probio/probio.htm)), then it follows that (1) probiotics must be live microbes; (2) probiotics must have data which document efficacy in the target host (not restricted to human use); (3) probiotics must be delivered at an effective dose. Implied is that probiotics must be safe and truthfully labeled with information on composition and viability through the end of labeled shelf life. The definition does not require that probiotics function through a specific mechanism (e.g. alteration of the intestinal flora), at a specific physiological site (for example, colon vs. stomach), be delivered through a specific route (oral vs. inravaginal) or through any specific product type (food vs. pharmaceutical).
- Validation of in vitro assays – it must be realized that often there is a presumption that certain assays (e.g., adhesion in tissue culture, production of antimicrobial compounds, resistance to bile and acid, survival through the intestinal tract) are required to demonstrate probiotic effects. For the most part, the scientific validation of the importance of these properties is not established.
- The results from a recently completed EU funded project (SYNCAN) were reported. This study showed that a synbiotic supplement (probiotics + prebiotic) significantly decreased some biomarkers for colon cancer in polyp and cancer patients, giving important support to the wealth of data from animal models. However, while dietary intervention studies of this type are very important to address anticancer effects of probiotics, they are still limited (with regard to making 'disease prevention' claims) as the biomarkers presently available are not validated.
- Both the in vitro and in vivo animal studies will support the human dietary intervention study. Various Biomarkers are analysed by the Biomarker Network.
- Vast evidence obtained by in vitro studies and animal models suggest a role for certain probiotics and also for prebiotics in the regulation of innate and acquired immunity. A series

of human studies on the usefulness of probiotics in chronic inflammatory conditions were reviewed during the conference. Controlled trials indicate that some probiotics are beneficial for the prevention and treatment of atopic dermatitis. Data on the prevention of necrotizing enterocolitis in newborns with low weight also suggest an important role of probiotics for this indication. Concerning inflammatory bowel diseases, there is only strong evidence of the benefit of probiotics in pouchitis and for maintaining remission in ulcerative colitis.

- The best documented health effect of probiotic strains comes from alleviation of episodes of diarrhea. Yet, with up to 90% of AIDS patients suffering from diarrhea, no concerted effort has yet been made to bring probiotic remedies to the developing world. Studies conducted in Africa were presented showing that yogurt supplemented with *L. rhamnosus* GR-1 can be safely used in HIV positive individuals and potentially not only resolve diarrhea but also increase a falling CD4 count. The enhanced eradication of bacterial vaginosis (a condition that increases the risk of HIV infection in women) using antibiotic plus probiotics and the development of a lactobacilli-based vaccine further illustrated potential benefits of probiotics for people around the world. With over 38,000 new cases of sexually transmitted infections reported in North America each day, no longer can developed countries ignore the massive societal destruction of HIV or think that it will not come to their shores. The globalization of probiotics to include people at the front line of poverty, malnutrition and diseases such as HIV/AIDS, has been raised by ISAPP in the past and continues to be strongly supported by the organization.
- The tools of functional genomics are beginning to be applied to probiotic organisms on a large scale. With multiple *Lactobacillus* and *Bifidobacterium* genomes sequenced in the past several years, we are gaining key insights into metabolic pathways and genetics of probiotic functions including immunomodulatory capacities. Several talks at the meeting described approaches for screening probiotic strains with respect to anti-inflammatory or immunomodulatory functions. The ability to perform comparative genomics, gene expression profiling, and proteomics will result in an enhanced ability to characterize established probiotic strains in detail and identify novel strains with specific probiotic functions.
- Research in the field of probiotic reaction with the immune system continues to evolve very quickly. New methods are being added to the palette of tools to study the cross talk between the flora and the host immune system. Advantage is taken from the increasing availability of genome sequences of lactic acid bacteria. Special attention was given to the importance of immune parameters in early life, and to the observed diversity of probiotics in their potential to influence the immune system. The concept that strains can and should be selected towards preset applications is gaining acceptance. This aspect was further elaborated in a discussion of the second generation probiotics: bacteria designed for an even better performance in the host. This involves strains with modified cell walls or secreting desired therapeutic molecules.
- Growth, processing and stabilization conditions can influence probiotic function. This is a largely overlooked aspect of evaluating probiotics for efficacy. Clearly, the phase of growth of the cells, the method of cell recovery from the fermentation, the method of recovery and preservation likely all impact the physiological state of the probiotic when consumed or applied to the host. It is likely, therefore, that these factors may also impact the ability of the probiotic to influence certain physiological traits in the target host. One concern about overlooking these issues is that publications on probiotics likely do not adequately describe these factors and will lack important information for interpreting studies.
- Yogurt can be a probiotic containing food, but it is not a probiotic.



ISAPP was also involved in a meeting sponsored by Danone regarding the start up of a Polish Probiotic Society. Held at the stately Grand Hotel in Krakow those interested in this society discussed how to approach development of such an organization. ISAPP does not sponsor chapters at this time, but we shared our philosophy that it is essential to promote, above all, the science of the area, and to define an appropriate and constructive role for industry involvement that does not interfere with this overarching goal. The vast contributions of industry scientists to advance the science in this field should be valued and encouraged in this proposed society, but in ISAPP's opinion, marketing and promotion of products is better left to other venues.

Those of us fortunate enough to participate in this Polish meeting thank the organizers and all the sponsors for this most enjoyable and rewarding conference.



## **Appendix C: Report from ISAPP-sponsored meeting in Africa**

INTERNATIONAL CONGRESS OF NUTRITION, 19-23 SEPTEMBER 2005, ICC, DURBAN,  
SOUTH AFRICA:  
NUTRITION SAFARI FOR INNOVATIVE SOLUTIONS

SUMMARY REPORT TO ISAPP

by Kingsley Anukam

University of Benin, Nigeria.

Unless you are a government official or big-time business mogul, applying for a visitor's visa to South Africa from Nigeria can be a difficult task. However, thanks to an ISAPP travel support letter and other supporting documents, I was able to obtain a visa. Moreover, thanks to support from ISAPP, I was able to fly to the conference, and many thanks to ISAPP Secretary, Dr. Gregor Reid, I was able to get safe and comfortable accommodation.

This is the first time that the Nutrition Congress has been held in Africa, and with over 3,500 delegates from all over the world, it was an impressive event. Hosting the Congress in Africa is timely and really challenged many stakeholders, policy makers and nutrition scientists, both from 'developed' and 'less developed' countries on the need to make a difference.

Listening to the South African Health Minister at the opening ceremony of the Congress, I was almost moved to tears as he passionately chronicled the extent of the impact of HIV/AIDS, poverty and malnutrition on the continent. I confess to wondering about whether or not the UN Millennium Development Goals in reducing hunger and food insecurity in a region under siege of HIV/AIDS can actually happen. There were a number of local and internationally renowned corporations at the conference exhibition stands, and many 'goodies' were on offer from grain bars to ice cream, yogurt, candies and drinks. Naturally, such companies are profit driven and this is understandable, but within the context of the opening speeches and the African setting, it saddened me that few foreign nationals are making any significant impact on the plight of people on this continent. Products tend to be high-end in cost, and not likely to bring profit levels met by sales in the developed world. The severe lack of probiotics in Africa is particularly concerning, as they clearly have an important role to play in ameliorating diarrhea and illness that plague the region.

Interestingly my poster presentation on the use of probiotic *Lactobacillus* GR-1 and RC-14 for the management of gastroenteritis of HIV/AIDS patients led to the gathering of 'Who is Who' in probiotics research at my stand, in addition to aid workers and African delegates who believe that probiotics can make a difference to the health and well-being of all citizens. This confirmed my perception that we need to collectively do more to bring the breakthroughs made in the developed world, to this continent. A food company that is based in the Netherlands discussed testing their probiotics on AIDS patients in a similar trial to the one I described. Time will tell if this comes to fruition. Although I have only tested 10 subjects, five with probiotics in yogurt and five placebo, it is clear that the probiotics have caused cessation of diarrhea, and we have preliminary data to suggest they can stabilize the depletion of CD4 counts. If the latter is confirmed, this will be an exciting development in the management of AIDS.

The concept of probiotics is an 'Old-New' idea that is gaining momentum across the world. Africa, from what I have seen, is willing to join in. This was exemplified by 3 out of 14 posters on probiotics were produced by African Scientists. At the probiotics symposium session, Dr.



Gregor Reid was excellent as the international chair. The audience of 250 heard about the importance of strain selection, product quality, properly performed clinical trials, the potential for synbiotics, and the mechanisms involved in immune modulation. It was a very good session, and ISAPP was creditably acknowledged.

The efforts of ISAPP to bring credibility to this area are to be applauded. It is not easy to change people's mindset and pioneer concepts that take society away from the drug therapeutic approaches that have prospered for the past 60 or so years. The next major challenge for ISAPP and its affiliated contacts, especially industry, is to integrate these teachings into the practical lives of people in Africa, and to lobby support for scientists to investigate local nuances of the microbiota.



## **Appendix D: Report from ISAPP-sponsored meeting in North America (AAM)**

American Academy of Microbiology Colloquium on Probiotic Microbes  
Report submitted by Gregor Reid

The American Academy of Microbiology hosted a colloquium on Probiotic Microbes on November 5-7 in Baltimore Maryland. ISAPP was one of the sponsors of this event and Dr. Gregor Reid represented the organization in the invitation-only workshop.

### **Format and outcomes**

Following some introductory presentations, the participants were split into three groups and asked to address a number of questions:

1. What are the consequences of normal flora acquisition?
2. What are the advantages to microflora manipulation?
3. What are the likely mechanisms for beneficial host-microbe interactions?
4. What are the likely mechanisms for beneficial microbe-microbe interactions?
5. Can we rationally identify probiotic candidates?
6. Regulatory issues.

A full report of the meeting will be written and made available on the web and in written form in around 6 month's time. It would be improper for me to publish a summary of the meeting ahead of the formal report, but in relation to ISAPP, the following comments representing my perceptions, may be of interest.

- The workshop format was excellent, and ISAPP's model of having experts discuss issues and interact closely, was proven again here to be an excellent means of running a workshop.
- The FAO/WHO definition of probiotics was upheld by the AAM, albeit after some discussion.
- Hot topics included creation and clinical use of recombinant strains; manipulation of the microbiota at birth compared to adulthood; a major need for clinical trials and condition-specific probiotics; use of genomics, proteomics and metabolomics to decipher the impact of probiotics (and prebiotics) on humans; and concerns over regulatory bureaucracy, pace, lack of guidelines and failure to properly adjudicate the area.

**In summary**, I believe this was an excellent forum for ISAPP to be represented. As seen from the list of participants, we did have good representation from people who have actively contributed to ISAPP in the past. Notably, the colloquium identified a number of others who should either be considered for participation in Coleraine, or who in time will become major contributors to probiotic and prebiotic research.



## Appendix E: Report from ISAPP-sponsored meeting in North America (IUMS)

### Symposium at 2005 meeting of the INTERNATIONAL UNION OF MICROBIOLOGICAL SOCIETIES July 27, 2005 San Francisco

#### ***Report filed by James Versalovic, Baylor College of Medicine, Houston TX:***

The 2005 meeting of the International Union of Microbiological Societies (IUMS) included the International Congress of Bacteriology and Applied Microbiology (ICBAM). As part of ICBAM, James Versalovic, MD, PhD, from Baylor College of Medicine chaired a session entitled "Probiotic Functions of Microorganisms" on July 27, 2005. Dr. Versalovic delivered the first lecture and included a brief discussion of ISAPP and its mission. He described studies of immunoprototics or the ability of probiotics to modulate host immune responses. Ultimately, specific probiotic strains may be useful for immunotherapeutic purposes. Karen Madsen, PhD, from the University of Alberta described the abilities of probiotic strains to reduce intestinal permeability and how probiotic DNA may modulate intestinal epithelial cell functions. Peter Lee, M.D., from Stanford University described his efforts to engineer *Lactobacillus jensenii* for the prevention of heterosexual transmission of HIV-1. Dr. Lee discussed the progress of his company, Osel Inc., regarding the expression of molecules that may block HIV transmission. Finally, David Pridmore from Nestle Inc. in Lausanne talked about the latest insights into the structure and biology of the genome of probiotic *Lactobacillus johnsonii* NCC 533.