2015 ISAPP Meeting Report
May 19-21, 2015
Georgetown University
Washington DC

CONTENTS:

I. EXECUTIVE SUMMARY

The 2015 ISAPP meeting was held on the Georgetown University campus in Washington DC. The venue was the Georgetown University Hotel and Conference Center. The popular Late Breaking News session featured 11 short, volunteered presentations on an array of topics including the correct pronunciation of "ISAPP" and use of probiotics from the perspective of economic benefit to society. The SFA poster session followed, which facilitated exchanges between the students and professional participants. The professional participants comprised 111 total delegates representing 19 countries (Australia, Bangladesh, Belgium, Canada, Denmark, Finland, France, Germany, Ireland, Israel, Italy, Japan, Netherlands, New Zealand, Singapore, Sweden, Switzerland, United Kingdom and United States). Sixty-one of the meeting participants were invited experts (including the eleven ISAPP Board members), 47 were industry members and 3 young scientists served as rapporteurs. Taking advantage of the program being in Washington DC, which facilitated regulatory and legal participation in the event, the first plenary session focused on regulatory restrictions in the United States on conducting human research on probiotics. The session featured presentations by an attorney, an FDA director and three clinicians. The second plenary session targeted two evolving areas of clinical intervention for probiotics and prebiotics: brain function and liver function. The final plenary was microbiome-oriented, exploring microbiome and evidence for causal role in health and disease. As usual for the ISAPP meetings, six discussion groups were held, on a range of topics (see section III). Some hot topics such as the need to update the prebiotic definition were hotly debated. Follow up from the meeting is expected to result in publications from all 6 discussion groups. A spectacular conference dinner was held at the National Academy of Sciences historic DC building, where Colin Hill was thanked for his past 3 years of service as ISAPP president, and Karen Scott was welcomed as the incoming president. Other events at the meeting included the Learning Forum – an educational session designed for ISAPP's Industry Advisory Committee members to go into depth on topics of emerging importance, and the wrap up session, in which chairs from each discussion group are allowed 20 min to recap highlights of their respective groups. The details of the 3-day program are found in Appendix A. The Student and Fellow Association conducted a concomitant meeting. This meeting would not be possible without the support of many companies and the hard work of many people; they are acknowledged in Appendix B.

II. WELCOME FROM THE PRESIDENT

Welcome all our invited scientists, IAC members and students and fellows to Georgetown University, Washington DC and to ISAPP 2015. This will be my last meeting as President and while I am delighted to be handing the role on to the very capable hands of Dr Karen Scott, I am also a little sad to think that I will no longer have the pleasure of acting as the figurehead of ISAPP. I choose the word 'figurehead' carefully rather than 'leader' because the ISAPP Board is fully stocked with leaders, all scientists who have achieved preeminence in their fields. Shrinking violets don't last long on the ISAPP Board and so my role has been somewhat ceremonial and focuses largely on timekeeping on our regular telecons. In any event, we are 'guided' in everything we do by our Executive Science Officer, Dr Mary Ellen Sanders, who has an extraordinary feel for the science, the regulatory and the commercial aspects of prebiotics and probiotics. As usual but with real feeling, I thank Mary Ellen on behalf of the Board for her outstanding efforts on behalf of ISAPP for yet another year.

It has been a very busy year (a summary of our efforts is detailed in the 2014 Annual Report[1] or in the 2014 Short Summary of ISAPP Activities[2]). It has been a challenging time for the public reputation and perception of prebiotics and probiotics, despite the increasing numbers of high quality scientific papers on the topic. We have tried to represent the science of prebiotics and probiotics to researchers, regulators and consumers. Partly this has involved publishing ISAPP-authored and -sponsored papers on a variety of topics, including a consensus paper on the scope and appropriate use of the term probiotic, which has been downloaded over 13,000 times since its publication last year. We have also made representations on behalf of the science to regulatory bodies (e.g. EFSA, FDA, CBER and FTC) and funded various educational events (sponsoring speakers to meetings, creating short videos together with the World Gastroenterology Organisation and collaborating on an updated version of the video, Microwarriors).

We have also put much effort into arranging this years' meeting in Washington, which as usual is set up as a mixture of plenary lectures and workshops which promote engagement of all the attendees and should allow lots of opportunity for vibrant discussions and time for renewing old friendships. In addition, 34 members of the Student and Fellow Association will present their research in a poster session. My thanks to Dan Merenstein, our local host, the Board members and other scientists who have agreed to co-chair our workshops and report back in plenary session on the last day. Thanks also to our very own Board member and ISAPP founder, Todd Klaenhammer, who has taken advantage of his membership in the National Academy of Sciences to organize our evening event on Wednesday in that august building on the Mall – a

[1] http://www.isapp.net/ISAPP-Highlights/Annual-Reports
[2] http://www.isapp.net/Portals/0/docs/Annual Reports/2014 ISAPP short summary.pdf

real honour (OK, honor since we are in the US) for which we are very grateful. It should be a really good night.

I conclude by thanking our industry colleagues from the IAC, who contribute so much to the science and the workshops and also persuade their parent companies to support ISAPP and keep us relevant in a changing world. We appreciate the support. I also thank Chris Cifelli and Saskia van Hemert for acting as IAC representatives to the Board.

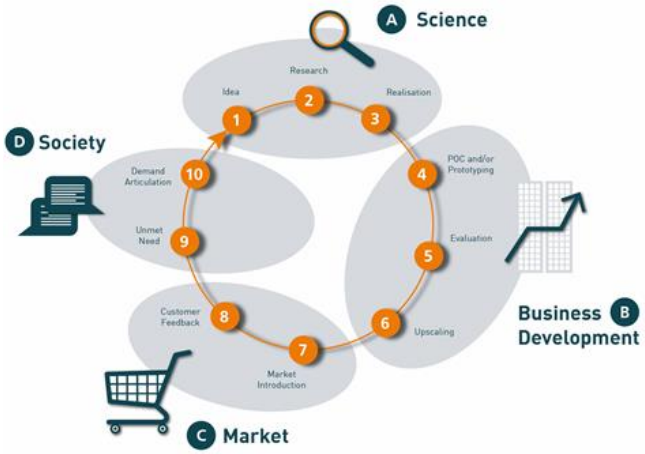
I wish you a productive and enjoyable meeting on the Georgetown University campus.

Colin Hill, President ISAPP

III. DISCUSSION GROUPS (Summaries submitted by group chairs)

Group 1. Technology transfer. Chairs: Michael Cabana and Eric Claassen

This work group focused on Technology Transfer and Academic Industry Partnerships. Eric Claassen, PhD discussed the cycle of new innovation (from science to business development to the market) and how this cycle leads to new innovation. Our group discussed several issues where this cycle does not proceed. For example, when academic investigators fail to pursue dissemination beyond the typical peer-reviewed publication (i.e., the knowledge paradox) or when there are multiple 'proof-of-concept' trials, without a commitment for further development (i.e., 'pilotitis'). Robert Kneller, MD, PhD, JD, from the University of Tokyo discussed his research on the role of small, start-up companies in developing new innovations in science. Finally, we discussed examples and ideas for Academic-Industry partnerships to deal with a variety of issues such as patent law, conflicts of interest, presentation of research results and control of data, among others. We learned about innovative approaches from Sally Cudmore, PhD (Alimentary Pharmabiotic Centre at the University of Cork), Jim Kiriakis, PhD (University of California, San Francisco Office of Innovation, Technology & Alliances) and Robert Al, PhD (Eindhoven University).



Group 1 Participants: Michael Cabana and Eric Claassen (Co-Chairs), Robert Al, Guenolee Prioult, Maurits van den Nieuwboer, Jim Kiriakis, Robert Kneller and Sally Cudmore.

Group 2. Prebiotics and oligosaccharides in the gut: who (is enriched), what (is the effect), where (do these effects occur), and how (are these effects ultimately manifested)? Chairs: Bob Hutkins and George Fahey

The main goal of the ISAPP Group 2 was to address the following fundamental questions: Which members of the gut microbiota are enriched, what are the effects, and where and how do they occur? Particular attention was devoted to next generation oligosaccharides, fibers, and polysaccharides that have prebiotic activity. The group also discussed whether or not a consensus panel should be convened to consider a new definition for "prebiotics". The main opposition to the latter question was based on the general satisfaction with the current definition as well as disagreements with the new definition recently proposed by Bindels et al., 2015.

Enrichment of particular members of the gut microbiota by prebiotics was noted in several presentations, but this was not the focus of our discussion. Rather, the consensus was that physiological effects, metabolic end-products (e.g., short chain fatty acids) and immune modulation were the more important and relevant outcomes of prebiotic consumption. In other words, enrichment of a particular strain, population or taxa is merely the means to an end. Defining mechanisms is clearly necessary, however, and connecting changes in the microbiota with physiological, biochemical, or immunological effects may provide mechanistic explanations for observed outcomes. Thus, identification of genes or pathways responsible for metabolism of prebiotics addresses this important need. Likewise, the development of rational synergistic synbiotics provides a basis for enhancing delivery of probiotic strains.

The group also noted that the host microbiota ultimately determines how effective prebiotics will be within an individual. In infants, for example, the ability to utilize human milk oligosaccharides depends on which specific members of the microbiota are present. Moreover, the molecular route by which oligosaccharides are metabolized (in infants as well as adults) may have profound effects (via cross-feeding) on other members of the microbiota. Indeed, the phenomenon of cross-feeding of prebiotics, milk oligosaccharides, plant fibers, and gut mucins is now recognized as having a large influence on the microbiota, whether for better or worse. However, identifying or predicting these effects is not easily assessed.

The group regarded many of these next generation prebiotics as having important nutritional (and commercial) potential. However, the group also noted that a critical limitation for the future of prebiotic research is the lack of chemistry capacity for identifying structures and quantifying specific molecular species (in food), as well as products following digestion. Ultimately, researchers will not be able to perform structure-function studies, metabolism studies, and mechanistic studies in the absence of an appropriate analytical chemistry infrastructure in glycomics.

The group also discussed where and how prebiotics act *in vivo*. While there are both luminal and epithelial effects, much more research is needed to identify the relative contribution of each. Mucin also has an important influence and provides a rich source of fermentable carbohydrate material, especially for *Bacteroides* and other colonic bacteria. Although more research is also needed to establish how prebiotic metabolism affects host health, considerable evidence has emerged emphasizing the function of SCFA and how they influence the immune system as well as various members of the microbiota. The anti-adhesive properties of prebiotics were also described, but whether they act *in vivo* at physiological-relevant concentrations has not been established. The group

noted the importance but did not discuss at length other means by which prebiotics might influence host health, including gut-brain axis and animal health.

Finally, the group endorsed the proposition that a multi-omics approach is necessary to understand the function of prebiotics in the gastrointestinal ecosystem and microbiota-host interactions.

Group 2 Participants: Bob Hutkins and George Fahey (Co-Chairs), Laure Bindels, Patrice Cani, Jun Goh, Bruce Hamaker, Janina Krumbeck (student rapporteur), Eric Martens, David Mills, Bob Rastall, Vincent Garcia Campayo, Rachel Buck, Coline Gerritsen, Margaret Haldeman, Arthur Ouwehand, Stephan Theis, Carl Volz, Elaine Vaughan

Group 3. Potential to employ probiotics/prebiotics for fetus and infants to improve well-being. Chairs: Seppo Salminen and Gregor Reid

Discussion topics

1. What do we know about nutrition, maternal stress, microbiome and fetal development?
2. What would be the basis for microbiota intervention at which stages of gestation?
3. How would we potentially enhance the gut and/or vaginal microbiota to pass certain microbes to baby at birth, and enhance infant formula or administer probiotics to breast-feeding mother, to influence post-natal development?

Summary points

Surprisingly, apart from overall calories, protein, calcium, iron, zinc and folic acid, there is no good understanding of the range of nutrients necessary for the development of different organs, vascular system, skeleton of the fetus, and none on the role of microbes and their metabolites from the mother or at the fetal-maternal interface. Nutrition is important during pregnancy to promote the health growth and development of the fetus , and nutrition counselling is clearly beneficial and along with exercise can reduce the risk of gestational diabetes. From the first to third trimester, the maternal gut microbiota become more diverse and the immune system becomes more inflammatory, the latter in a process required for birthing.

Imaging tools, such as fMRI, are being developed which could potentially provide insight into the fetal structural and functional development of various organs, with the brain, heart, pancreas and liver of particular interest. Methods can track auditory and organ development (e.g. neural tubes), but the process is expensive, requiring lengthy times when the fetus (or infant) is quiet for image acquisition.

Evidence of the importance of the microbiota in reproduction comes from studies showing lactobacilli involvement in sperm motility and depletion of these organisms in failure of *in vitro* fertilization.

Stress is clearly a factor in poor pregnancy outcomes. Susceptibility to stress may be itself set up in early life with maternal –infant separation a clear risk factor in animal and human studies and human studies of attachment. Two studies were conceived to examine stress. For the Developed World, the effects of post-traumatic stress--for example through life events, partner abuse, car accidents, military combat--could be examined with levels of environmental chemicals tested salivary cortisol (e.g. neurochemical levels in urine) and gut microbiota and metabolome documented. In case relevant data are available from the pre-shock period, natural experiments can also be undertaken in populations exposed to natural or man-made catastrophic disruptions in daily life. The role of chronic exposure to environmental toxins in fetal and maternal health has not been adequately studied and is a global issue. Follow up of such a study should be long term (>25 years) to assess development and outcomes such as adult educational attainment employment and relationships. Chronic malnutrition is an additional factor in the Developing World, and a study was proposed for Bangladesh, with monitoring of dietary intake and partner abuse included.

Interventions

Based upon existing information and clinical documentation, there is sufficient reason to propose the use of probiotics before, during and after pregnancy.

Pre-conception:

- Use a combination of *Lactobacillus brevi* cd2, *L. salivarius* fv2, and *L. plantarum* fv9 to improve sperm motility and viability.

- Use orally administered *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 to reduce recurrence of bacterial vaginosis (BV).

After conception:

- Continue with GR-1/RC-14 to prevent BV and preterm labour, and reduce uptake of environmental toxins.
- Potentially for more aggressive treatment of BV, *L. crispatus* CTV05, after it becomes approved.
- Chewing gum or lozenge of *Lactobacillus reuteri* for oral health in an attempt to prevent periodontitis and lower the risk of preterm labour.
- Oral *Bifidobacterium lactis* BB-12 and *L. rhamnosus* GG from week 20 to reduce the risk of overweight and gestational diabetes and until 6 months post-partum of breastfeeding for infants at risk of allergic disease and to reduce uptake of environmental toxins.
- *Bifidobacterium breve* and alpha linolenic acid maternal intake during the 3rd trimester with a view to improving fetal neural development.
- *Lactobacillus salivarius* from week 20 to improve breast milk microbiota.
- For women intending to have an elective c section, we may give mother and infant *B. infantis* / *B. longum* for one week before delivery and the infant for six months.

For infants:

- For premature infants, various *Lactobacillus* GG and *Bifidobacterium* BB12, *B. longum infantis* to reduce the risk of necrotizing enterocolitis, and *L. plantarum* to reduce risk of neonatal sepsis(developing world?). Preferably these strains would be added to breast milk or given between feeds.
- Supplement pasteurized donor milk with probiotic *L. rhamnosus* GG (as in Finland) and *B. infantis and B. breve*

There seemed to be consensus that it made sense to develop a means to supplement with specific nutrients and microbes at different stages of infancy. Data are needed on prebiotic interventions Affordable, stable probiotics are needed for low income countries.

Transcriptomic and metabolomics studies are needed to better understand how the organisms work in a given niche. Health monitoring by blood or urine analysis, is also recommended to assess potential effects on neurochemicals and brain health.

In conclusion, there are enough reasons to suggest that probiotic lactobacilli and bifidobacteria could improve pregnancy outcomes and provide a safe supplement from before, during and after pregnancy, and for the early life of the infant. No such cocktail of strains has ever been developed for this purpose, so either it would need to be tested, or a series of products would need to be used, although the Group was not necessarily stating that the evidence for the regimen proposed, has been duly tested and verified.

Group 3 Participants: Gregor Reid and Seppo Salminen (Co-Chairs), Andrea Roberts, Kaouther Ben Amor, Jodi Bettler, Howard Cash, Rhodri Cusack, Gabriele Gros, Flavia Indrio, Islam Khan, Himanshu Kumar (SFA), Mark Lyte, Bo Mollstam, Pirjo Nuutila, Pinaki Panagrahi, Bruno Pot, Samuli Rautava, Margriet Schoterman, Catherine Stanton, Dan Tancredi, and Jacinta Tobin.

Group 4. What is the future of probiotics in the USA? Regulatory challenges. Chairs: Dan Merenstein and Mary Ellen Sanders

The intent of this discussion group was to understand the challenges of the current regulatory approach to human research on probiotics in the USA and to discuss ways to move research forward. The discussion group comprised a diverse group of stakeholders, including clinical experts, researchers, federal government officials, research funders, lawyers and industry experts.

The discussion was extremely positive. There was largely agreement that at least some of the current regulatory requirements imposed on probiotic research hindered research progress and increased cost without improving study subject safety. Many examples were given that demonstrated clearly how regulatory delays have stalled research. Additionally, it was noted that research being conducted is often compromised when study designs and outcomes measured are manipulated to enable studies to conform to regulatory requirements. The approach has put US researchers at a disadvantage globally.

The key discussion points and challenges centered on the following issues:

- Despite FDA's efforts to clarify the regulatory status of clinical investigations of probiotics, problems remain in this area. In this regard, the September 2013 Investigational New Drug (IND) guidance and February, 2012 FDA final guidance "Early Clinical Trials with Live Bio-therapeutic Products: Chemistry, Manufacturing, and Control Information" are still under FDA review. A Federal Register notice requesting comments on the latter guidance was published at the end of March 2015.
- FDA currently requires an IND in many circumstances, even when the intent is human studies of commonly used foods and dietary supplements.
- When INDs are required, safety studies are often required, even when potentially relevant data on safety exist or the subject of the research is a product that has been widely consumed for many years.

The discussion resulted in support for the following measures that would facilitate US progress with human probiotic research:

- The degree of regulatory oversight should balance study subject vulnerability and documented safety for the intended use for the probiotic strain.
- A reassessment by FDA is needed about when an IND for probiotic research would be required. Any new drug development research would require an IND, but a path for human research on probiotic foods (including all subcategories of foods) not under an IND should be possible.
- Not all probiotic human research is necessarily under the jurisdiction of CBER; CFSAN can also play an important consultation role/resource for safety assessment when research is on foods, dietary supplements, medical foods and foods for special dietary uses that are either commercial or under development.
- When an IND is needed, an abbreviated IND process for probiotic products with well characterized chemistry, manufacturing, and controls (CMC) and accrued evidence of safety should be an option.
- The proposal by CBER put forth for public comment (Federal Register Notice) would ease the path to conducting research under an IND on commercialized probiotics by allowing the product label to serve as CMC information.
- A requirement to conduct a safety study before any efficacy studies should depend on the information available and should not be automatically triggered.

- Evidence of probiotic strain safety (including safety evaluations from other countries, history of safe use, scientific evidence, GRAS evaluations, NDINs) should be considered in determining the need for a safety study, regardless of the research endpoint.
- Better interagency communication between CBER and CFSAN is needed. A single point of contact with both CBER and CFSAN or a cross-center committee should be designated to serve as a resource for researchers and industry seeking to conduct human probiotic research. This would assist in the process of determining if an IND is necessary for the research, and if so, facilitate the IND process.

Some of these suggestions are counter to the FDA's guidance issued September of 2013 regarding very broad requirements for human research to be conducted under an IND. As mentioned, portions of that guidance are under review.

Another important point raised during the discussion was that the regulatory category of a substance is dictated by intent of vendor, not study endpoints. There seemed to be agreement among the attorneys present about this. However, input from regulators was not provided on this matter.

Group 4 Participants: Dan Merenstein, Georgetown University Medical Center and Mary Ellen Sanders, ISAPP (Co-Chairs); Pat Hibberd, Massachusetts General Hospital, Boston; Andi Shane, Emory; Richard Oberhelman, Tulane; Girish Deshpande, Nepean Hospital Sydney; Peter Marks, FDA CBER; Chris Elkins, FDA CFSAN; Jennifer Patro, FDA CFSAN; Linda Duffy, NIH-NCCIH; Martin Hahn, Hogan Lovells; Sarah Roller, Kelley Drye & Warren LLP; Diane Hoffmann, University of Maryland; Tina Tan (rapporteur), Georgetown University; Greg Leyer, UAS; David Keller, Ganeden Biotech; Maeve Murphy, General Mills; Solange Henoud, Lallemand Health Solutions; Thomas Tompkins, Lallemand Health Solutions; Berenice Ocampo Guevata, Mead Johnson Nutrition; Seema Mody, DSM; Danielle de Montigny, BioK+; Wafaa Ayad, Church & Dwight; Akito Kato, Yakult USA.

Group 5. Intestinal barrier function – its role in GI disease, allergy, and other diseases. Chair: Eamonn Quigley and Todd Klaenhammer

1. What are the biggest research gaps?

a. What are the unanswered questions in relation to interactions between the microbiome and the barrier?

The concept of the gut barrier has been grossly oversimplified in the medical and lay literature with an almost exclusive focus on the single layer of epithelial cells and of the tight junctions that unite them. The barrier and its associated defense mechanism incorporates multiple components such as the various mucus layers, molecules secreted by the epithelium and, of course, the mucosal immune system. All of these can interact with the microbiome.

A key issue regarding barrier-bacterial interactions is the primacy of gut barrier changes in relation to the microbiome. Which comes first, an altered microbiome or an impaired barrier, or are they both simultaneously affected by a third, primary factor or insult? Studies of the microbiome also need to move beyond descriptions of quantitative and qualitative observations of microbial populations to an examination of their putative or actual functions using metagenomics, metabolomics and allied technologies.

b. What are the limitations in translating in vitro and animal work to man?

While detailed and precise assessments of the morphology and function of the barrier can be performed using *in vivo* in animal models, such precision is not possible in man and great caution must be maintained when extrapolating from animal work to the interpretation of the relatively blunt instruments employed in human studies. Even more caution must be exercised in interpreting *ex vivo* and *in vitro* work. These typically focus on one component of the barrier and fail to detect the dynamic interactions that undoubtedly occur between its constituent members. Most misleading have been conclusions related to tight junction function and dysfunction; claims for the passage of large and complex molecules across tight junctions are simply untenable based on what we know about their size and function. When it comes to studies of the impact of probiotics on barrier function, a number of additional issues arise, including variability in probiotic strains employed, use of different animal models and the relative scarcity of high quality human studies. A fundamental issue with all animal studies to date is distinguishing association from causation. Rarely, has this been possible.

2. What diseases/health conditions are associated with compromised gut barriers?

a. In these disorders is gut barrier dysfunction a primary abnormality or a secondary phenomenon?

Abnormalities in intestinal barrier function have been described or ascribed to a host of disorders, often on the basis of nothing more than mere conjecture. The lay press and internet chatter is replete of references to “leaky gut” syndrome, a vague and poorly delineated concept usually promulgated on the basis of no data. Impaired barrier function manifests through increased intestinal permeability and has been well described in relation to excessive alcohol consumption as well as numerous health conditions, including: celiac disease, inflammatory bowel disease, diarrhea predominant irritable bowel syndrome (IBS-D) and post-infectious irritable bowel syndrome (PI-IBS), many forms of liver disease, and metabolic syndrome.

Impaired barrier function may play a fundamental role in some disorders, as suggested by its documentation in otherwise healthy first-degree relatives of patients with celiac and inflammatory bowel disease. Further support for the role of intestinal barrier function in inflammatory bowel disease (IBD) comes from the description of gene polymorphisms linked to barrier function in some individuals with IBD. It is also possible that a subset of subjects with IBS-D or PI-IBS may have a primary abnormality in permeability as evidenced by changes in expression of microRNA-29a, a regulator of membrane permeability in some subjects with D-IBS, as well as by direct studies of permeability in subjects with IBS.

In many instances, the primacy of changes in permeability to disease expression is difficult to define and it remains likely that several of the disorders listed above may reflect interactions between genetic predisposition and environmental stressors (including an altered microbiome).

3. What novel techniques are being developed to measure or provide insight into gut barrier integrity?

a. Is the measurement of gut barrier function in man sufficiently robust and reproducible to detect defects in disease as well as the impact of therapeutic interventions?

While all techniques that have been proposed to measure permeability in man have their limitations, and each seems to measure something different, there appears s to be a consensus that the lactulose:mannitol ratio is widely accepted as the best validated model. A normal range has been defined for this test but within- and between-subject variability is substantial, as evidenced by the considerable overlap that inevitably occurs between diseased and normal populations. There remains a concern that this approach may not be sufficiently sensitive to detect changes in response to a given intervention. Ideally, a suite of tests should be employed, providing the broadest picture possible of epithelial function. Additional approaches may include Ussing chamber studies of intestinal biopsies and assays of mir29a or other circulating markers of permeability.

4. Is the gut barrier a valid target for interventions that modify the microbiome?

A large volume of animal work has clearly demonstrated (in relation to alcoholic and non-alcoholic liver disease, for example) that interventions, such as probiotics, can restore gut barrier function in validated models of these disorders, and provided a biological basis for these effect. The interpretation of barrier function in human studies continues to be complicated by many confounders such as the effects of diet, saturated fatty acids, alcohol, and NSAIDs, so it is unclear whether a probiotic treatment could have a disease-modifying effect in these disorders. Benefits in terms of symptom improvements (e.g. resolution of diarrhea), which have been noted with probiotics in a number of disorders, could be related to a barrier effect. While there is no doubt that the gut barrier represents a valid target and interventions, such as probiotics, are worthy of investigation. However, it remains unclear whether the reproducibility and the sensitivity of available tools to measure permeability are sufficiently robust to provide meaningful data at this time, necessitating the use of multiple methods for the most accurate assessments.

Group 5 Participants: Eamonn Quigley and Todd Klaenhammer (Co-Chairs), Jerrold R. Turner, Nathalie Delzenne, Wenke Feng, Reuben Wong, Thierry Piche, Irina Kirpich, Brant Johnson (rapporteur).

Group 6. The microbiome response to pre/probiotics. Chairs: Karen Scott and Glenn Gibson

The group debated several issues around this overall theme and made the following conclusions.

Effect of probiotics and prebiotics on indigenous intestinal microbiota. How can the effects be measured?
In terms of determining the efficacy of a prebiotic or probiotic in healthy individuals, it is important to correlate functionality of the microbiota (e.g. metabolite production) with changes in microbial composition. In such cases, efficacy should be measured as the ability of a pro/prebiotic(s) to maintain a 'healthy' intestinal ecosystem by direct inhibition of pathogen activity, immunomodulation and/or the production of useful metabolites (e.g. organic acids, vitamins). However, in cases where pro/prebiotics are being used to mitigate the effects of a disease, efficacy may be more appropriately measured by reduction of clinical symptoms e.g. reduction in gastrointestinal pathogens, improved inflammatory status and reduction of incidence and severity of necrotising enterocolitis, antibiotic-associated diarrhoea and symptoms of obesity/metabolic syndrome. We concluded that both probiotics and prebiotics could influence the indigenous intestinal microbiota – both in species composition of the microbial population and in the metabolic activities of these microbes. However, the intervention (strains, fermentable substrate) used, dose applied, host diet, targeted human population and targeted site of action can all influence outcomes.

How relevant are samples? - faeces vs gut.
In both humans and pigs, it is recognised that the faecal microbiota is not reflective of more proximal gastrointestinal areas. Human faecal samples have been shown to possess a markedly different microbiota than samples from the various sites in large intestine – including the most distal part of the intestine, the rectum. Additionally, a probiotic challenge study in pigs using five lactobacilli species revealed that different species were dominant in the ileum than in faeces.. However, once one acknowledges these limitations, faeces can be a useful surrogate marker that is easily accessible, enabling researchers to gather a large number of samples, without the need for significant clinical expertise. The task, as we see it, will be in determining appropriate faecal biomarkers that can be used as measure of intestinal health.

What is the relative importance of contributions from different omics techniques?
As mentioned, functionality of the microbiota is key. Combining data from multiple omics techniques (e.g. marrying metabonomics with metataxonomics results from the same sample) elucidates relationships between the presence or absence of certain species, genes or proteins with desirable metabolic outputs. This would enable the rational design of probiotic and prebiotic interventions that would drive the metabolic output of the microbiota in a manner that improves human health.

Which human populations should be targeted with pro/prebiotics?
Changes in the gut microbiome are apparent with age and pro/prebiotic influences are likely to vary because of this. Persons 'at risk' of disorder (e.g. metabolic syndrome) as well as those with existing clinical states (e.g. IBS, IBD) may benefit from interventions. Malnutrition and antibiotic treatment are further special cases where pro/prebiotics may help. Due to the inherent inter-individual variation of indigenous intestinal microbiota, stratification of individuals into responders and non-responders may reduce data heterogeneity and clarify results.

Extensive analysis of the intestinal microbiota over the last two decades has revealed several indigenous bacterial species that may elicit a significant effect on the intestinal ecosystem. These bacteria include

Akkermansia muciniphila, Faecalibacterium praustnizii, Ruminococcus bromii, Roseburia/Eubacterium rectale and Oxalobacter formigenes, and may be developed into a new generation of probiotics. Similarly, new prebiotics may be developed to fortify these taxa.

Conclusions:

- Probiotics and prebiotics can affect the commensal microbiota – with caveats as discussed
- Faecal samples are an acceptable surrogate for changes in the large intestine
- Microbiota changes are only one marker of efficacy - need to consider alternatives
- Alternative 'omics tie together activity and composition
- Different populations require different approaches – infants, teenage, pregnant disease, elderly
- Gut microbiota research has revealed several species from indigenous microbiota that may be developed into a new generation of probiotics

Group 6 Participants: Karen Scott and Glenn Gibson (Co-Chairs), Paul Sheridan, Julian Marchesi, Lindsay Hall, Omry Koren, Anne Salonen, Yuan-Kun Lee, Paul O'Toole, Maria Marco, Colin Hill, Rodney Dietert, Gun-Britt Fransson, JoMay Chow, Valerie Benoit, Lori Lathrop Stern, Marie-Emmanuelle Le Guern, Sylvie Binda, Koji Nomoto, Benedicte Flambard, Juliet Ansell**.**

IV. IAC LEARNING FORUM PROGRAM

The Learning Forum is a program that was started to specifically address learning gaps of ISAPP industry members. The IAC members are surveyed to determine topics they would like to see addressed either in more depth than is typically possible in a 25 min plenary lecture or with a range of experts, who can discuss different aspects of a complex topic.

The 2015 Learning Forum focused on 2 topics:

- Meta-analyses: Considerations for probiotics and prebiotics studies, presented by Daniel J. Tancredi, PhD, UC Davis Department of Pediatrics and Center for Healthcare Policy and Research (CHPR), Sacramento, CA
- Using neuroimaging to study the effects of probiotic and prebiotic on the human brain, presented by John VanMeter, Ph.D., Dept. Neurology, Director, Center for Functional and Molecular Imaging, Georgetown University Medical Center, Washington DC.

Meta-analyses: Meta-analyses are statistical methods to synthesize evidence from separate studies. Coupled with a well-done systematic review of the literature yielding combinable studies, effective meta-analyses produce transparent, systematic, objective and accurate assessment of the effects of experimental interventions. Hence, systematic reviews and meta-analyses are emerging as a preferred approach by scientists and policymakers for evaluating and synthesizing evidence. However, weaknesses in the individual studies or in the methods used in the systematic review and meta-analysis can lead to faulty conclusions. In this seminar, Daniel Tancredi, PhD, will provide a general overview of how meta-analyses are performed and enumerate important study design, analysis and reporting considerations for scientists and their sponsors engaged in probiotics and prebiotics research. In addition, Dr. Tancredi will identify controversies with how meta-analysis methods are currently applied when individual probiotic/prebiotic studies vary in their assessed outcomes or in the dosage, strain or composition of the interventions being compared.

Neuroimaging: The neuroscience community has until recently largely ignored the effect that the human microbiome can have on the central nervous system and in particular the link between the gut and brain via microbiota. In last few years, several studies have demonstrated how changes in gut microbiota can affect neuropsychological disorders and neurological diseases. These studies have demonstrated how microbiota can affect postnatal development of hypothalamic–pituitary–adrenal (HPA) stress reactivity in germ-free mice (Sudo et al., 2004), reverse age-related deficits in long-term potentiation (the basis of memory) through a mixture of eight different probiotics (Distrutti et al., 2014), and reduce visceral pain in animal models using probiotics (Rousseaux et al., 2007). Further, a range of probiotics has been shown to reduce anxiety and improve performance on a complex maze task (Matthews and Jenks 2013); normalize anxiety-like behavior in a colitis model (Bercik et al., 2011); and normalize infection-induced anxiety (Bercik et al., 2010). Recent studies are beginning to use neuroimaging techniques such as structural MRI to measure changes in the number of multiple sclerosis lesions (Fleming 2011) and functional MRI (fMRI) to directly study the effect of probiotics on emotional reactivity (Tillish et al., 2013). In this talk I will discuss how neuroimaging techniques can be used to directly assess the effect of probiotics and prebiotics on the human brain.

V. LATE BREAKING NEWS

2015 Late Breaking News Session
2015 ISAPP Meeting
Georgetown University, Washington DC
Tuesday, May 19, 3:30-4:35 PM, Salon CH, Georgetown University Hotel

Chair: Gregor Reid, University of Western Ontario, Canada

This session is an opportunity for people to give short presentations (5 min) on late breaking news topics in an informal, interactive atmosphere. These presentations range from 'hot' off-the-bench news from lab/clinic to controversial or important issues on the science, politics, funding, business or humorous aspects of the field of probiotics or prebiotics.

Schedule for 2015 Late Breaking News session

	First name	Surname	Affiliation	Title
3:30	Troup	John	Metagenics	Practitioner & patient education for the selection and use of effective probiotics
3:35	Kiran	Thakur	National Dairy Research Institute, India	Probiotic lactic acid bacteria as a vitamin supplier to human consumers
3:40	Gibson	Glenn	University of Reading	What's in a name?
3:45	Johnson	Brant	North Carolina State University	Identification of S. Layer associated proteins (SLAPS) in *Lactobacillus* reveals new avenues for studying probiotic-host interactions
3:50	van Hemert	Saskia	Winclove	Can probiotics be used as preventative strategy for depression
3:55	Reid	Gregor	University of Western Ontario	Probiotics for preterm babies - the issues
4:00	Grimaldi	Roberta	University of Reading	Fermentation properties and potential prebiotic activity of a high purity GOS on in vitro gut microbiota parameters in healthy individuals
4:05	Rains	Tia	Egg Nutrition Center	Interests in joining ISAPP
4:10	Nuutila	Pirjo	University of Turku	Metabolic disease, microbiota and imaging of intestinal metabolism
4:15	Mills	David	University of California, Davis	Select probiotics prevent pathogen growth driven by commensal glycan degradation – probiotic-assisted colonization resistance
4:20	Piche	Thierry	Gastroenterology, CHU NICE	Translational approaches to study epithelial barrier integrity
4:25	Singh	Satvinder	All India Institute of Medical Sciences	Propionate: friend or foe
4:30	Ouwehand	Arthur	Dupont/Danisco	Probiotics provide public health and economic benefits to society

VI. STUDENTS AND FELLOWS ASSOCIATION PROGRAM (Prepared by Gregor Reid)

The Students and Fellows Association (SFA) of ISAPP held another successful conference in Washington DC between 18-20th May, 2015, with over 30 students and fellows from 11 countries. The Executive consisted of Juhani Aakko as President, and Laure Bindels, Samantha Stone, Jordan Bisanz, Himanshu Kumar and Maria Maldonado-Gomez as Executive Members.

The program had highlights of a two hour poster session with active participation from ISAPP attendees, and short talks from SFA members. Being able to hear the excellent plenary talks and ISAPP wrap up were also highlights, along with interacting with students, fellows and ISAPP attendees. However, there was too much spare time on the first morning, and a thief spoiled the poster session by stealing two laptops. This was clearly an 'in house' job, and the 'security' at the hotel was incompetent. A major negative was the very poor and unsafe accommodation arranged for the students, by a 'local' SFA member who didn't even attend the event. This will not be allowed to happen again, and local representatives must be more engaged and accountable, and accommodation checked by ISAPP personnel ahead of time.

All the SFA attendees would have liked to have been at the ISAPP group meetings, but logistically this was not possible.

The "Career in Academics and Industry Session" benefitted from four ISAPP speakers, with David Mills cited as being excellent. However, there was a feeling that this session is getting stale, especially for SFA members who have been to more than one event. A more participatory event, such as workshops, will be planned for 2016. A few talks were given by the students/fellows, and this was appreciated by all. Any mechanism whereby all SFA attendees can speak would be a bonus if logistically feasible. The degree of interest at the poster sessions meant there was little time for SFA members to visit posters of their colleagues. Next year, posters will be put up for longer to allow even more interaction.
The Facebook/blog activity has dried up, and needs to be reinvigorated to provide a year-round forum for interaction. A problem arose in that 4 students/fellows from India did not show up at the meeting. Initially, there was concern that they had used the forum to enter America illegally, however, this was dispelled later by Dr. Reid writing to them and their supervisors. There also appeared to be some students/fellows who did not attend the whole event. These actions have led to some major re-thinking about organizational aspects of the meeting, with guidelines being developed to prove travel arrangements have been made ahead of the meeting, rooms booked by each person, and commitments made within a timeframe so that replacements can be invited with sufficient time.

The travel allowance provided by the IAC through ISAPP is very generous and appreciated. However, given the high level of interest of students and fellows to attend each year, it makes it difficult to know how best to distribute the funds. For next year, the amounts awarded will be revisited, with perhaps fewer students coming long distances but given more support, and more emphasis placed on attendees who live closer to the event site.

The SFA meeting is an outstanding opportunity for students and fellows to organize their own conference and interact with scientists at the top of their discipline. I feel that more appreciation is needed by SFA members of the Executive and Dr. Mary Ellen Sanders, and the time and effort they put into the organization. In future, this will be recognized by issuance of certificates.

Jean Macklaim from London, Ontario has been chosen as the President for 2015-16, and her task will be to improve the organizational and archival aspects of the SFA, including having meeting minutes collated and distributed, clear channels of communication within and outwith SFA/ISAPP, a more dynamic meeting program, and clearly demarcated jobs for all Executive members. She, and other Executive members, will work closely with me to insure the SFA goes from strength to strength. Everyone is excited about the Turku event.

Rafael Segura from University of Nebraska reviews his poster with ISAPP invited expert, Jim Kiriakis

Students, academic participants and ISAPP industry members network during poster session.

Wafaa Ayad and Mary Ellen Sanders share conversation during the Welcome Reception.

Patricia Hibberd delivers lecture during Plenary Session 1.

Dan Merenstein, Sarah Roller and Girish Deshpande field questions during panel discussion in Plenary Session 1.

Peter Marks (2nd from right) answers question from audience, while other panelists, Dan Merenstein, Sarah Roller and Girish Deshpande listen.

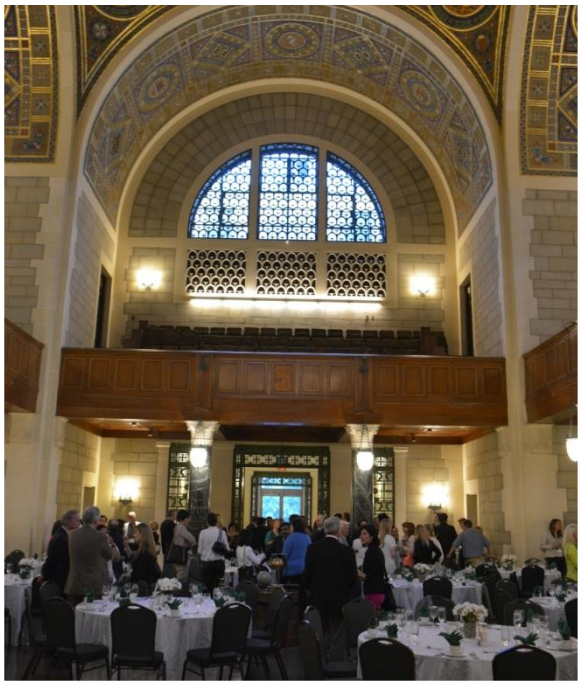
Sarah Roller listens to response to her question during Plenary Session 1.

Eamonn Quigley (L) fields questions after his presentation "Influencing the liver and implications for obesity and metabolic syndrome." Gregor Reid chairs.

Eamonn Quigley (L) and Mark Lyte during panel discussion of Plenary Session 2.

Rodney Dietert (L) fields questions after his presentation "Health and disease aspects of the human microbiome" in Plenary Session 3. Glenn Gibson chairs.

Yuan-Kun Lee, National University of Singapore, presents his lecture, "How the microbiome is influenced by diet and ethnicity."



ISAPP Gala Dinner at the Great Hall, National Academy of Sciences.

Outgoing ISAPP President, Colin Hill, speaks about his 3-year tenure at ISAPP president.

National Academy of Sciences member and evening host, Prof. Todd Klaenhammer, welcomes ISAPP to the Great Hall of the National Academy.

Nathalie Delzenne, Catherine Stanton, Paul O'Toole, Janina Krumbeck and Laura Bindels enjoy dinner and comradery at the National Academy of Sciences.

Incoming ISAPP President Karen Scott (R) welcomes all to the Gala Dinner at the National Academy of Sciences. Mary Ellen Sanders applauds.

ISAPP participants gather for a photo at the National Academy of Sciences.

WRAP UP SESSION:

Karen Scott, Group 6
Gregor Reid, Group 3

Bob Hutkins, Group 2
Dan Merenstein, Group 4

APPENDIX A. PROGRAM FOR THE ISAPP MEETING

2015 ISAPP Meeting
Program
May 19-21, 2015
Georgetown University Hotel and Conference Center (GUHCC)

Tuesday, May 19, 2015
9:00 – 11:00 AM **Registration**
9:00 AM-Noon **Student and Fellow Association program.** Chair: Juhani Aakko, University of Turku, Finland
9:00-11:00 AM **Break**
9:00-11:00 AM **Board of Directors meeting.** Chair: Colin Hill, Alimentary Pharmabiotic Centre, Ireland
10:00-11:00 AM **Industry Advisory Committee meeting.** Chair: Christopher Cifelli, National Dairy Council
11:00 AM–Noon **Board of Directors + Industry Advisory Committee meeting.** Chair: Colin Hill
Noon–1:00 PM **Lunch**
1:00-3:00 PM **IAC Learning Forum**. Chair: Chris Cifelli PhD *1:00-2:00 PM* Meta-analyses: Considerations for probiotics and prebiotics studies. Daniel Tancredi PhD, UC Davis School of Medicine *2:00–3:00 PM* Using neuroimaging to study the effects of probiotic and prebiotic on the human brain. John VanMeter MD, Georgetown University
3:30-4:30 PM **Late Breaking News** (with refreshments). Chair: Gregor Reid
4:30-6:30 PM **Poster Session and Welcome Reception**
Wednesday, May 20, 2015
7:00-8:00 AM **Breakfast**
7:15-10:00 AM **Registration**
8:00 AM **Welcome**. Colin Hill PhD, President ISAPP and Daniel Merenstein MD, local host *8:15 – 10:00 AM* **Plenary session 1. Regulatory challenges to moving probiotics forward in the USA.** Chairs: Daniel Merenstein MD, Georgetown University Medical School and Mary Ellen Sanders PhD, ISAPP Executive Science Officer *8:15-8:30 AM* Introduction. Daniel Merenstein MD *8:30-9:30 AM* Insights to lead to solutions: • U.S. Regulation of Probiotics: Can FDA Make Room for Another Way? Sarah Roller JD, RD, MPH, Kelley Drye & Warren LLP, Washington DC • Regulatory perspectives on human research on probiotics. Peter Marks MD, FDA Center for Biologics Evaluation and Research • Frontline perspective from a physician. Pat Hibberd MD PhD, Massachusetts General Hospital • Finding a solution: probiotics for premature infants. Girish Deshpande FRACP, MSc (CEpid),

Nepean Hospital Sydney, Australia *9:30-10:00 AM* Panel discussion: How do we move probiotics forward considering regulatory approaches to probiotics in the USA?
10:00-10:30 AM **Break**
10:30 AM-Noon **Plenary Session 2. What's needed to translate pro/prebiotics to clinical outcomes?** Chairs: Gregor Reid PhD, Lawson Research Institute, Canada and Eamonn Quigley MD, The Methodist Hospital and Weill Cornell School of Medicine, Houston *10.30-11.00 AM* Evaluating the potential of probiotics and prebiotics for influencing brain function - from fetus to adults. Mark Lyte PhD, Texas Tech University, Lubbock *11.00-11.30 AM* Influencing the liver and implications for obesity and metabolic syndrome. Eamonn Quigley MD *11.30 AM-noon* Open discussion
Noon **Box lunches for working lunch in discussion group rooms**
Noon – 6 PM **Breakout discussion groups**
1. Technology transfer. Chair: Michael Cabana and Eric Claassen
2. Prebiotics and oligosaccharides in the gut: who (is enriched), what (is the effect), where (do these effects occur), and how (are these effects ultimately manifested)? Chairs: Bob Hutkins and George Fahey
3. Potential to employ probiotics/prebiotics for fetus and infants to improve well-being. Chairs: Seppo Salminen and Gregor Reid
4. What is the future of probiotics in the USA? Regulatory challenges. Chairs: Dan Merenstein and Mary Ellen Sanders
5. Intestinal barrier function – its role in GI disease, allergy, and other diseases. Chair: Eamonn Quigley and Todd Klaenhammer
6. The microbiome response to pre/probiotics. Chairs: Karen Scott and Glenn Gibson
2:30-3:30 PM **Break**
1:00-5:00 PM **Student and Fellow Association program**
6:30 PM **Conference Dinner**. Buses depart at 6:30 PM from near hotel; return by 10:00 PM
Thursday, May 21, 2015
7:00-8:00 AM **Breakfast**
8:00-9:30 AM **Plenary Session 3. Modulating the microbiome**. Chairs: Karen Scott PhD, University of Aberdeen, UK and Glenn Gibson PhD, University of Reading, UK *8:00-8:30 AM* What evidence exists for a causal role of the microbiome in human health and disease? Bringing 'omics techniques together. – Julian Marchesi PhD, Cardiff University, UK *8:30-9:00 AM* Health and disease aspects of the human microbiome. Rodney Dietert PhD, Cornell University, New York, USA *9:00-9:30 AM* How the microbiome is influenced by diet and ethnicity. Yuan-Kun Lee PhD, National University of Singapore
9:30-10:00 AM **Break**
10 AM – 12:30 PM **Wrap Up** (20 min x 6 group reports). Chair: Todd Klaenhammer PhD, North Carolina State University
12:30-1:30 PM **Lunch**
2:00-4:00 PM **Board of Directors meeting.** Chair: Karen Scott

APPENDIX B. ACKNOWLEDGMENTS

This meeting would not be possible without the support and hard work of a large group of people and companies, acknowledged here.

IAC partners (led by Chris Cifelli and Saskia van Hemert)
ISAPP is fortunate to be sponsored by probiotic and prebiotic companies around the globe, who value research and discovery. Through their generous support, ISAPP has the funds to conduct its annual meetings. ISAPP expresses appreciation for the support provided by the 38 2015 IAC companies.

Abbott Nutrition
Beneo/Suedzucker AG Mannheim
Biocodex
BioGaia AB
BioK+ International
Cargill, Inc.
CDRF
Chr. Hansens
Church & Dwight
Clasado Limited
Coscura Groupe Warcoing SA
Danisco Sweeteners Oy Dupont
Danone Research
DSM/i-Health
Egg Nutrition Center
FrieslandCampina Innovation Center
Ganeden
General Mills Inc
Kimberly-Clark Corporation
Lallemand Health Solutions, inc.
Mead Johnson Nutrition
Merck
Metagenics
Mondelez
National Dairy Council
Nestec, S.A.
NIZO
Nutricia Research
Pfizer Consumer Healthcare
Probi
Probiotics International Ltd. (Protexin)
Procter & Gamble
Sensus-Royal Cosun
UAS Laboratories LLC
Valio
Winclove Bio Industries
Yakult Honsha Co.
Zespri

ISAPP Board
Colin Hill (President), Karen Scott (Vice-President), Michael Cabana (Secretary), George Fahey (Treasurer), Glenn Gibson (Past President), Todd Klaenhammer, Gregor Reid, Seppo Salminen, Eamonn Quigley, Dan Merenstein and Mary Ellen Sanders (Executive Science Officer). IAC representatives (non-voting) to the board: Chris Cifelli and Saskia van Hemert.

Instructors for the IAC Learning Forum:
Daniel Tancredi PhD, UC Davis School of Medicine
John VanMeter MD, Georgetown University

Discussion group chairs, especially non-board members:
Bob Hutkins
Eric Classen

APPENDIX C: 2015 ISAPP MEETING PARTICIPANT LIST

IE: Invited expert; IAC: Industry Advisory Committee; BoD: Board of Directors member

Last Name	First Name	Affiliation	ISAPP affiliation
Al	Robert	Framework Support	IE
Ansell	Juliet	Zespri International Ltd	IAC
Ayed	Wafaa	Church & Dwight	IAC
Barlow	Janine	Probiotics International Ltd	IAC
Ben Amor	Kaouther	Danone Nutricia Research	IAC
Benoit	Valerie	General Mills	IAC
Bettler	Jodi	Nestle Nutrition	IAC
Binda	Sylvie	Danone Nutricia Research	IAC
Bindels	Laure	Universitie catholique de Louvain	IE
Bosscher	Douwina	Cargill	IAC
Buck	Rachael	Abbott Nutrition	IAC
Cabana	Michael	University of California, San Francisco	BoD
Cani	Patrice D.	Universitie catholique de Louvain	IE
Cash	Howard	Ganeden Biotech, Inc.	IAC
Chow	JoMay	Abbott Nutrition	IAC
Cifelli	Chris	National Dairy Council	IAC
Claassen	Eric	Vrije Universiteit Amsterdam Athena Institute	IE
Contractor	Nikky	Metagenics	IAC
Cudmore	Sally	Alimentary Pharmabiotic Centre	IE
Cusack	Rhodri	Brain and Mind Institute, Western University	IE
Delzenne	Nathlaie	Universitie catholique de Louvain	IE
Deshpande	Girish	Nepean Hospital Sydney, University of Sydney	IE
Dietert	Rodney	Department of Microbiology and Immunology	IE
Fahey	George	University of Illinois at Urbana-Champaign	BoD
Fargier	Emilie	Biocodex	IAC
Feng	Wenke	University of Louisville	IE
Flambard	Benedicte	Chr. Hansen	IAC
Fransson	Gun-Britt	Probi AB	IAC
Garcia Campayo	vicenta	Cargill	IAC
Gerritsen	Coline	Winclove Probiotics	IAC
Gibson	Glenn	University of Reading	BoD
Gross	Gabriele	Mead Johnson Nutrition	IAC
Hahn	Martin	Hogan Lovell US LLP	IE
Haldeman	Margaret	i-Health, Inc.	IAC
Hall	Lindsay	University of East Anglia & Institute of Food Research	IE
Hamaker	Bruce	Purdue University	IE
Henoud	Solange	Lallemand Health Solutions Inc.	IAC
Hibberd	Patricia	Massachusetts General Hospital	IE

Hill	Colin	APC Microbiome Institute	BoD
Hoffmann	Diane	University of Maryland School of Law	IE
Holmgren	Kerstin	Probi AB	IAC
Hutkins	Bob	University of Nebraska	IE
Indrio	Flavia	UNIVERSITY OF BARI DEPT OF PEDIATRIC	IE
Jacobs	Heidi	Cosucra Groupe Warcoing S.A.	IAC
Janusz	Michael	Procter & Gamble	IAC
Johnson	Brant	North Carolina State University	IE
Kato	Akito	Yakult U.S.A. Inc.	IAC
Keller	David	Ganeden BIotech	IAC
Khan	Ashraful Islam	International Centre for Diarrhoeal Disease Research	IE
Kiriakis	Jim	University of California San Francisco	IE
Kirpich	Irina	University of Louisville	IE
Klaenhammer	Todd	NC State University	BoD
Kneller	Robert	University of Tokyo, RCAST	IE
Koren	Omry	Bar Ilan University	IE
Krumbeck	Janina	University of Nebraska, Lincoln	Rapporteur
Kumar	Himanshu	Functional Foods Forum,	Rapporteur
Lathrop Stern	Lori	Pfizer Consumer Healthcare	IAC
Le Guern	Marie-Emmanuelle	Biocodex	IAC
Lee	Yuan-Kun	National University of Singapore	IE
Leyer	Gregory	UAS Labs, LLC	IAC
Lyte	Mark	Texas Tech University Health Sciences Center	IE
Mackle	Tami	Pfizer Consumer Healthcare	IAC
Marchesi	Julian	Cardiff University/Imperial College London	IE
Marco	Maria	University of California, Davis	IE
Marks	Peter	U.S. Food and Drug Administration/Center for Biologics Evaluation and Research	IE
Martens	Eric	University of Michigan Medical School	IE
Merenstein	Dan	Georgetown University	IE
Mills	David	University of California	IE
Mody	Seema	DSM	IAC
Mollstam	Bo	BioGaia AB	IAC
Murphy	Maeve	General Mills Inc	IAC
Nomto	Koji	Yakult Central Institute	IAC
Nuutila	Pirjo	Turku PET centre, University of Turku	IE
Oberhelman	Richard	Tulane School of Public Health and Tropical Medicine	IE
Ocampo Guevata	Berenice	Mead Johnson Nutrition	IAC

O'Toole	Paul	University College Cork	IE
Ouwehand	Arthur	DuPont Nutrition & Health	IAC
Panigrahi	Pinaki	University of Nebraska Medical Center	IE
Patro	Jennifer	CFSAN	IE
Piche	Thierry	Gastroenterology, CHU NICE, FRANCE	IE
Pot	Bruno	Institut Pasteur de Lille	IE
Prioult	Geuenolee	Nestle	IAC
Quigley	Eamonn	Houston Methodist Hospital, Weill Cornell Medical College	BoD
Rains	Tia	Egg Nutrition Center	IAC
Rastall	Robert	Department of Food and Nutritional Sciences, University of Reading	IE
Rautava	Samuli	Department of Paediatrics, University of Turku	IE
Reid	Gregor	Lawson Health Research Institute	BoD
Roberts	Andrea	Harvard School of Public Health	IE
Roller	Sarah	Kelley Drye & Warren LLP	IE
Roos	Stefan	BioGaia AB	IAC
Salminen	Seppo	University of Turku	BoD
Salonen	Anne	Universtiy of Helsinki	IE
Sanders	Mary Ellen	ISAPP	BoD
Schoterman	Margriet	FrieslandCampina	IAC
Scott	Karen	Rowett Institute of Nutrition and Health	BoD
Shane	Andi	Emory University School of Medicine	IE
Sheridan	Paul	Rowett Institute	IE
Stanton	Catherine	TEAGASC Moorepark Food Research Centre and Alimentary Pharmabiotic Centre	IE
Tan	Tina	Georgetown University	Rapporteur
Tancredi	Daniel	Associate Professor in Residence of Pediatrics, University of California, Davis	IE
Theis	Stephan	BENEO Institute	IAC
Tobin	Jacinta	University of Melbourne	IE
Tompkins	Thomas	Lallemand Health Solutions inc.	IAC
Troup	John	Metagenics	IAC
Turner	Jerrold	The University of Chicago	IE
Tzortzis	George	Clasado Inc	IAC
van den Nieuwboer	Maurits	VU University Amsterdam	IE
van Hemert	Saskia	Winclove Probiotics	IAC
Vaughan	Elaine	Sensus BV (Royal Cosun)	IAC
Volz	Carl	Sensus BV (Royal Cosun)	IAC
Wong	Reuben	National University of Singapore	IE