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BOOK REVIEW

Bioactive foods in promoting health: probiotics and prebiotics

R.R. Watson and V.R. Preedy (editors)

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'By use of probiotics people can dramatically expand their exposure to protective chemicals and thus readily reduce their risk of multiple diseases' according to the preface of the above book. However, which of the bacteria or bio-molecules that they produce best prevent disease or promote health? This book tries to answer these questions by focusing on probiotics and their role in bio-modulation of natural products to produce active agents from inactive molecules in dietary fruits and vegetables. The book aims to be the most current and concise scientific appraisal of the efficacy of pro- and prebiotics in preventing disease and improving quality of life. It reviews, but also presents new hypotheses and conclusions on the effects of the bioactive components of probiotics to fight disease and improve the health of various populations. It contains 638 pages, divided into 5 sections with 35 chapters.

Overview

The first section with 6 chapters gives an introduction and overview of the field. In the first chapter the production of probiotic cultures and their incorporation in foods is discussed. A chapter such as this is usually missing from books dealing with probiotics, while it is actually one of the most important aspects that lead to ingestion of viable microorganisms. It is unfortunate that the chapter is brief, and gives only a few examples of how to increase survival of probiotics, e.g. by incorporating them in calcium alginate beads. Also, the paragraphs on simulated gastrointestinal tract conditions need more attention. Nevertheless, it is a subject that should be present in every handbook on

probiotics. The authors also define a new concept, that of a probioactive, which is defined as a metabolite that is produced by probiotics as they grow in a food matrix. These probioactives have health effects which are generally hypothesised to be different from the immunomodulating capacities (which are usually through cell-wall components) of probiotics. (which are usually through cell-wall components). The second chapter gives an overview of new and emerging prebiotics and of probiotics used in foods (without actually listing the probiotics). Some of the efficacy and safety studies generally performed for pre- and probiotics are listed as well. There is a specific section in this chapter on claims for pre- and probiotics, which is a welcome addition in these times where most dossiers are not approved by EFSA. The third chapter is a very brief, 3-page, historical perspective on probiotics. It is useful for those that do not know this history, but the information could perhaps have been incorporated in Chapter 2. The fourth chapter deals with the safety of probiotic bacteria. As I have stated in previous book reviews, this is an important aspect that is usually overlooked. It partly overlaps with a similar section in Chapter 2, but this is more extensive and lists cases where safety has been an issue. The contribution of Kiseleva *et al.* (Beneficial Microbes 2: 139-154) in this issue on the potential of probiotics to induce autoimmune disease shows that this is something that cannot be ignored. The fifth chapter deals with an overview of the prevention of infections by probiotics, in my opinion the most proven benefit of these beneficial microbes. These infections range from necrotising enterocolitis (NEC) in children, diarrhoea and other gastrointestinal disorders, to urogenital

infections. The last chapter of this section gives an overview of the benefits of pro- and prebiotics in human health. Going through the chapter there is significant overlap with previous chapters in this section and more detailed information in the other sections. I have the impression that the order and content of the chapters could have done with a little more editorial mingling.

Prebiotics in health promotion

The second section of the book is entitled 'Prebiotics in health promotion' and contains 4 chapters. The first chapter in this section deals with the effects of prebiotics (and probiotics) on liver function. Actually, most of the data available is on probiotics and only a limited number of studies have been carried out with prebiotics. These include the effect of FOS (fructo-oligosaccharides) on liver injury after endotoxic shock and sepsis, and the effect of beta-glucan, inulin, pectin or resistant starch (in the presence or absence of a cocktail of probiotics) on cirrhosis, hepatic encephalopathy and liver transplantation. A clear benefit of prebiotics has been their inclusion in infant formulas. This is discussed in Chapter 8. However, the chapter not only focuses on the benefits, but also lists the risks of including prebiotics in infant formula, an angle that is rarely looked at in publications from more commercial contributions. Since 'the neonatal period is a critical period of development when microbes become established in the gastrointestinal tract, the long-term effects of manipulation of the gut microbiota during this time' requires caution in perinatal and neonatal infants. Also, the authors recognise that dose is important in tolerance, where a high dose results in excessive flatus, borborygmi, abdominal pain and diarrhoea (editorial note: this is also true for adults). The subsequent chapter continues along the same lines with prebiotics as infant foods. There is substantial overlap between this and the previous chapter. The last chapter in this section deals with the effects of prebiotics in the gastrointestinal tract. Although brief, it describes the effects of prebiotics in inflammatory bowel disease (IBD) and cancer, which are the disorders that are most studied using prebiotics. However, the author has also included thoughts on the use of prebiotics in the aging gut. In a (Western) world with an increasing elderly population this is a new aspect that needs to be expanded.

Pre- and probiotics as therapies

The third section, with 5 chapters, is entitled 'Prebiotics and probiotics as therapies'. Along the lines of EFSA and other regulatory bodies, this would mean that they would be used as drugs, rather than foods, but the chapters in this section show that there are benefits in the treatment of various disorders as well. Unfortunately, Chapter 11, the first chapter in this section, deals with both prevention and treatment of pre- and probiotics in allergic asthma.

The data on prevention is clear for certain strains, that for treatment is almost non-existent. Chapter 12 deals with a role for pre- and probiotics in surgery recuperation. This is a refreshing chapter and in my opinion this field requires more attention. The rationale given by the authors for the use of probiotics is that 'new strategies should be developed' to combat postoperative infections. That for prebiotics is weaker, as their use 'seems reasonable due to their (editorial: = pro- + prebiotics) effects at the mucosal barrier setting'. The chapter lists some convincing examples of how both can be used to minimise complications after surgery. I have heard several other cases studies described during recent conferences that allow me to believe that there is potential for both in this area. Chapter 13 deals with both therapy and prevention of gastrointestinal diseases in children. This is one (of the most) thorough chapter(s). It describes immune effects, acute gastroenteritis, antibiotic associated diarrhoea (AAD), *Clostridium difficile* infection, travellers' diarrhoea, irritable bowel syndrome (IBS), constipation, IBD, *Helicobacter pylori* infections, colic and regurgitation, and NEC. Where available, both treatment and prevention are discussed. The next chapter, chapter 14, covers the effects of pre- and probiotics and diarrhoea. It is unfortunate that various other chapters have also dealt with this already, although not in as much detail as in chapter 14. It is a well-written chapter, which concludes that prevention, abatement or shortening of rotavirus-induced or AAD are considered to be well-established probiotic effects. The authors remind the reader that due to strain, matrix, and target group specificity (infant, adults, elderly, patients, etc.) variable, contradictory or even negative effects can be observed. This is in line with my editorial in the previous issue of Beneficial Microbes (volume 2, issue 1, pp 1-7). The last chapter in this section is on probiotics and AIDS. There have been only a limited number of studies in this area. The authors conclude that the proof of probiotics in the prevention of HIV infection needs to be further studied, but since probiotics might have immunostimulatory properties, it is worthwhile investigating this.

Probiotics and health

The fourth section in the book is entitled 'Probiotics and health'. It is the largest section, with 15 chapters. However, the chapters dealing with bioengineering of bacteria and microarray analysis of probiotic effectiveness don't really seem to fit. The first chapter, Chapter 18, deals with the exciting area of the effects of (pre- and) probiotics in metabolic disorders and obesity. I have a personal weakness for this subject, particularly in studying the role of the microbiota in energy harvesting from prebiotics. This is a well-written chapter by two experts in the area. It critically discusses the evidence of the effects of pre- and probiotics, or the combination of the two. The authors conclude that 'so far only a few trials have demonstrated that the administration of probiotics, prebiotics and their

combination (synbiotics) exerts moderate positive effects *in vivo*. Nevertheless, the results obtained might help us improve our knowledge and design better strategies to treat and prevent obesity and the associated metabolic disorders. Chapter 19 is a brief one on probiotics and *H. pylori*. It describes the different ways in which probiotics might influence *H. pylori* infection, from direct antimicrobial activity to indirect ways by decreasing gastric inflammation. The next chapter discusses the evidence of probiotics in neonatal sepsis associated with NEC and meningitis. There is some evidence that the strain LGG may be beneficial and the chapter focuses on this strain. It is therefore unfortunate that in their conclusion the authors state that 'probiotics' (in general) might be beneficial, since it is now well known that data from one strain cannot be used to generalise the effects of all probiotics. The well-established effect of (pre- and) probiotics on atopic eczema (AE) is discussed in Chapter 19. Here, a lot of studies have been performed on the prevention, but also on treatment of AE. I would have grouped this chapter with Chapter 11 on the effect of pre- and probiotics on allergic asthma. The available data is critically discussed and the authors conclude that especially during the first 2 years of life, AE may be reduced by selected pre- and probiotics. Pregnant women are advised to take probiotics (specifically LGG) in late pregnancy and during the first 6 months after delivery, provided that they breast-feed. Therapeutic use to improve AE is only supportive in infants under 18 months of age.

Chapter 20 deals with bioengineering of probiotics to improve their effects. The chapter gives some impressive examples of the effect of improved, designer probiotics, but the use of genetically modified probiotics is far from being established (both within the regulatory world as well as within society). Nevertheless, these types of experiments may help in screening large collections of strains for those strains with the required bioactive molecule, and this may result in the selection and production of new probiotics. Chapter 21 is a chapter dealing with one of the proposed mechanisms through which probiotics may be beneficial: by modulation of intestinal transport and epithelial barrier function. It describes the *in vitro* and animal studies that can be performed to assess this, and discusses the different molecular pathways that may be involved. However, even in the single clinical trial that I know of that has investigated expression of proteins involved in epithelial barrier (proteins of the tight junction) in humans, it was unclear whether upregulation of these proteins in the duodenum of the human volunteers actually led to an improvement in barrier function, as this could not be established in the same experiment. Also, EFSA does not think that expression of these or other markers *per se* means that the epithelial barrier is improved. Therefore, the clinical relevance is not yet clear. Chapter 22 deals with food processing and food formulations to increase probiotic activity or numbers in the gastrointestinal tract. Despite the fact that

the addition of prebiotics might actually lead to a lower survival of probiotics, depending on the concentration (Venema, Beneficial Microbes 2: 1-7), addition of other components or simply adding probiotics to fruits, for example, might affect their survival due to the presence, amongst other things, of inhibitory factors in these foods. This is described here, although the focus is more on factors that increase probiotic survival in the final food product. Another mechanism of probiotics is discussed in Chapter 23: diminishing adhesion of pathogens. Models to test adhesion are described. The assessment of adhesion properties of the probiotic isolates as well as competitive exclusion of adhesive pathogens is an important attribute in probiotic characterisation. However, the authors caution that preclinical results and *in vivo* results do not always correlate. For example, strains that show similar adhesion *in vitro*, may adhere to a different degree, or some may not adhere at all, *in vivo*. This is partly due to the limitation of the models that are used for these tests.

Chapter 24 describes the effects of probiotics on fungal colonisation of the gastrointestinal tract. Apart from the mostly discussed lactic acid bacteria and bifidobacteria, this chapter also includes examples of *Saccharomyces boulardii*. Mechanisms may vary from production of antifungal substances to immunomodulation (both cellular and humoral). Chapter 25 deals with health claims and evidence. The chapter lists 26 single strain and 9 multi-strain probiotics with 'proven health benefit' in the categories digestive health, protection and others. Proven has been defined here as showing benefit in clinical trials. I am quite sure that the more stringent criteria applied by EFSA would drastically reduce this list. Health claim systems in Japan, China, Brazil and Europe are discussed in detail. It is unclear why the US system is excluded. A weak point is that for the Chinese system health claim categories and product names are given using Chinese characters. Chapter 26 discusses the evidence of probiotics in heart health. The effects of probiotics on hypertension and hypercholesterolemia are discussed. The effects of hypertension are not a direct effect of probiotics, but are brought about by the action of probioactives, namely the production of bioactive peptides from milk proteins. The mechanisms of cholesterol reduction are still a matter of debate. The effect of food pathogens on cardiac health is also discussed, as foodborne pathogens have been associated with carditis and other forms of heart damage. The following chapter is another chapter on infant nutrition. It completely overlaps with the other two chapters addressing this, and also discusses prebiotics in a section devoted to probiotics.

Another chapter, Chapter 28, that is misplaced in this section deals with microarray analyses of probiotic effectiveness. It is also far from clear how these analyses can be correlated to actual health benefits if these are not measured in the same experiments. An interesting chapter

is on probiotics in cancer prevention. Effects may be caused by immunomodulatory or non-immune mechanisms. These latter may correspond to cell turnover and proliferation, and cell death. Chapter 30, the last chapter in this section, deals with the effects of probiotics on IBS. In the developed world approximately 20% of the population is affected, but the pathogenesis of the disorder remains poorly understood. The chapter gives a comprehensive overview of the clinical trials that either showed or failed to show an effect when probiotics were given. Two strains, *Bifidobacterium infantis* 35624 and *Escherichia coli* DSM 17252 have been shown in more than one trial to reduce symptoms in IBS.

Animal models to study probiotics

The last section in the book describes animal models for studying probiotics (although some of the chapters have included prebiotics as well), and contains 5 chapters. The first describes human microbiota-associated animals as a model for studying the effects of pre- and probiotics. These models are a useful substitute for human volunteers for a number of obvious reasons, but as a model they also have some limitations. An important one is that gastrointestinal conditions in these animals are not the same as in man. Moreover, although not mentioned by the authors, the microbiota that establishes in these animals deviates significantly from that of the human individual. Nevertheless, they are undoubtedly a better model than the same animal with its natural-associated microbiota. The next chapter describes the use of probiotics in fish much more than the use of fish as an animal model, which the title of the section would lead one to expect. This is the

only chapter that describes the usefulness of probiotics in animal feeds, and is as such out of place, although it is a well-written chapter. Chapter 33 describes animal models and their use in studying the effects of prebiotics. The chapter gives much more of an overview of prebiotics than animal models. Given the title of this section of the book, this chapter should perhaps have been placed in the overview-section, or the title of this section should have been on pre- and probiotics. The last two chapters of this section deal with colitis models. There is substantial overlap in graphics, tables and references and the editors should have fused these two chapters. Nonetheless, a nice overview of the various animal models, e.g. knock-out mice, that are available to study the effects of probiotics is presented. Together they describe the lessons learned from these models and allow the generation of hypotheses with respect to mode of action of particular probiotic strains. At present, evidence exists only for the prevention and maintenance of remission of pouchitis. Treatment with probiotics alone for pouchitis is not effective.

Conclusion

In conclusion, I consider this book to be helpful reading material. Most of the chapters have been written by scientists who are not immediately the most well-known. This gives a refreshing view on the field. As intended, the book does put forward some hypotheses that are not generally discussed in the pre- and probiotic arena. However, the book lacks proper editorial management, as there is a lot of overlap between separate chapters, and titles of sections are not well chosen in my opinion.

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BOOK REVIEW

Probiotics and health claims

W. Kneifel and S. Salminen (editors)

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'Probiotics have a long history in nutrition and medicine, but their health benefits have been demonstrated only more recently, when proven standards of clinical assessment have been applied' according to the preface of the book. This has contributed to the scientific basis for the establishment of health claims associated with probiotic products. A need for objective regulation of these claims has arisen, to prevent the marketing of (over-the-counter) products that claim effects that have not been proven with that particular product. The contributions in this book are written by renowned experts and cover different scientific areas and viewpoints, and the text aims to be a helpful source for a broad spectrum of scientists with current multidisciplinary expertise in this field. It can also be used to compare different regulatory systems used in different parts of the world, as each are individually discussed in the book. It contains 360 pages, divided over 20 chapters.

Historical overview

The first chapter is entitled 'Probiotics and health: from history to future'. Amongst other things, it describes the contribution of such famous scientists as Doderlein, Tissier, Metchnikoff and Nissle to the use of microorganisms for medicinal purposes. The highlights of findings over the past 35 years have been addressed in this chapter. Current evidence for benefits in lactose intolerance, inflammatory bowel disease (IBD), gastroenteritis (acute, antibiotic-associated, travellers' or *C. difficile* diarrhoea), cholesterol lowering, urogenital infections, allergies, dental caries, and treatment and prevention of cancer are discussed. Furthermore, some other, more recent medical applications are also listed, such as benefits in autoimmune disease,

diabetes, graft-versus-host disease and radiation side effects. The section on future developments and use of probiotics is interesting and discusses the use of probiotics as platforms for the delivery of drugs, enzymes, hormones, and (micro)nutrients. As an example the IL-10-producing *Lactobacillus lactis* is given. It should be noted that these strains will be genetically modified (GM), and should be considered drugs and no longer food (supplements). Toxin sequestration and carcinogen detoxification are other future developments listed, even though there have been examples of these in the past. Specific cases of platforms for drug or enzyme deliveries that are mentioned are GM strains expressing antibodies to neutralise pathogens, or GM strains that produce enzymes to treat enzyme deficiencies. The author concludes that these developments may provide new applications and provide probiotics with an important role in the 'armamentarium against the multiple diseases and disorders that afflict humankind'. The second chapter describes the world's oldest (commercial) probiotic, *Lactobacillus casei* Shirota (LcS), isolated in 1930. It describes the challenge of (in this case) Dr. Minoru Shirota to bring the research from theory to practice. As early as the 1960s and 1970s the first clinical trials with LcS were performed. The chapter describes well-documented examples of beneficial modulation of the gut microbiota (so far EFSA in Europe has not approved claims on this), improvement of stool consistency, reduction of production of putrefactive metabolites, protection from infection, immune modulation activity, and the prophylactic effect on bladder cancer development. The first health claim on a product containing LcS was approved in Japan in 1998. This related to improved microbiota balance and improved intestinal milieu. Subsequent claims were approved in

Brazil (2001), Taiwan (2003 and 2008), China (2004) and the Netherlands (2006). Most are related to improved microbial balance and bowel habit (in subjects susceptible to constipation). The mechanisms of action could be multiple, varying from host-microbe cross-talk, to bacteria-bacteria interactions, or modulation of the gut microbiota. During 75 years of sound scientific research, this is one of the best studied probiotic strains.

Probiotics: from strain to product

An important aspect in probiotic research is that claims should be submitted on products containing the probiotics, not on the strains themselves. In fact, the (food) matrix in which the probiotic strain(s) are present may have an effect on their survival and efficacy (Venema, 2011. *Beneficial Microbes* 2: 1-7). Chapter 3 describes the route to formulating the food product in such a way that it facilitates survival of the included probiotic. Apart from their health beneficial properties, technological properties of probiotic strains may be equally if not more important. Producing probiotics on a large scale and adding them to various food products such as fermented milk products, cheese, and fruit and vegetables juices are discussed in this chapter. Especially challenging are dried products (e.g. probiotics in capsules, or sachets), that should ultimately deliver live probiotic cells to the gastrointestinal tract of the human individual consuming such products. Chapter 4 describes the challenges for tailoring their efficacy. A first assessment in addition to good functional and technological properties is safety of the strains in use. Even if the current safety of most products is well established, probiotics could, as living microorganisms, theoretically be responsible for side effects in susceptible individuals. In fact, a number of cases have been described in the recent past. Thus, safety should remain an important consideration. The authors also describe in this chapter a number of ways in which to improve the assessment of probiotic functionality, ranging from *in vitro* models (cell cultures, or those mimicking the gastrointestinal [GI] tract), to animal trials (conventional or germ-free models, and knock-out animals), and even clinical trials. Also discussed are ways to improve stress-resistance of probiotics, to increase their survival in food production and in the GI tract. These include the application of sub-lethal stress, immobilised cell technology, (micro)encapsulation technology, and genetic engineering. To improve the specificity of probiotics the authors put forward suggestions on combinations of strains, nutritional manipulation by, for example, prebiotics, as well as genetic engineering. A new generation of probiotics is foreseen with strains like *Faecalibacterium prausnitzii* with anti-inflammatory activity, lactate-dissimilating strains such as *Eubacterium hallii*, or probiotics controlling the accumulation of hydrogen.

Probiotics and health claims

The next 6 chapters (Chapter 5-10) deal with various aspects of probiotics and health claims. The first describes a European and Brazilian perspective. Basic concepts such as appropriate identification and nomenclature of strains, as well as safety assessments are discussed, as is the 'totality of supporting evidence'. The total evidence should demonstrate: (1) the extent to which the effect is relevant for health; (2) a cause-effect relationship, with a focus on consistency and specificity of the effect, dose-response, and biological plausibility of the relationship; (3) the amount of the product required to obtain the effect; and (4) the target population. Specific challenges for probiotic products include proof of viability of the strains at the moment of ingestion, the set-up of clinical trials with the proper controls and target population. The next chapter describes the US perspective. Importantly, the author states how the term probiotic is often misused. Only those strains which (a) are alive when administered; (b) have been proven to have beneficial effects in clinical trials; and (c) are safe, can be considered probiotics. Most researchers will call any strain with potential a probiotic. This is something that I pay close attention to in manuscripts submitted to *Beneficial Microbes* as well. The chapter goes on to describe the different types of claims that can be applied for in the US: structure/function, health and medicinal claims. It lists the key considerations for substantiation of such claims. A much-welcomed section deals with bridging the gap between the (US) consumer and probiotic science and commercial products. This section describes how the International Scientific Association for Probiotics and Prebiotics (ISAPP) has prepared consumer guidelines for choosing probiotic products. Chapter 7 discusses a specific case in the US regarding 'reduced cardiovascular disease risk'. It does not focus on probiotics. In fact, I was unable to find this phrase in the chapter. Chapter 8 describes the Japan perspective. With FOSHU, Japan was the first to introduce regulation on health claims (on probiotics). Fifteen probiotic strains carry a FOSHU claim in Japan, with *B. lactis* Bb-12 carrying multiple claims. Approved FOSHU claims for probiotics include those on the strain reaching the intestines alive, increasing the numbers of beneficial microbes, promoting or maintaining a good intestinal milieu, maintaining good GI condition, or reducing harmful bacteria. As a comparison, of these claims EFSA has not yet been able to approve a single dossier, likely due to the stricter requirement upheld by EFSA. Chapter 9 displays the China perspectives on regulation. In China it is unclear whether a functional food should be considered a health food or a medicine. A health food is defined as a food with a specific health function, but not meant to cure a disease. No clear guidelines have been published and companies need to consult the appropriate regulatory bodies on a case-by-case basis. The new Food Safety Law of 2009 states that 'Medicines cannot be added to food,

unless the added substance is traditionally considered both food and Chinese medicine'. Apart from this discussion, issues regarding preparation of dossiers are similar to that in other countries. The next chapter describes the Indian perspective. Regulation on probiotics in India is still not clear. Guidelines are proposed on a website and stakeholders are invited to provide comments. Of note is that a special clause for the use of indigenous strains is mentioned. It is stated that probiotics of foreign origin should be evaluated in an Indian population prior to their use in India. Furthermore, a need for the development of indigenous probiotic strains for optimal functionality in the gut microbiota of Indian populations is postulated.

What is required for obtaining an approved health claim?

At present, certainly in Europe, it is not always entirely clear which (clinical) data are sufficient to get an approved health claim. Chapter 11 describes the role of meta-analyses in evaluating clinical trials on probiotics. Almost all areas in which probiotics have shown functionality have been studied using meta-analyses, including all forms of diarrhoea, IBS, IBD, several infections, allergy and constipation. The major argument against pooling data from several different strains is that effects are clearly strain-dependent, and the effects of one strain can be greater, or even contradictory to those of another strain. This, to me, carries more weight than the argument that by pooling trials, the sample size and power is increased. If the pooling of trials is the only way to show that probiotics have a significant effect, then it must be clear that the effect is either small or non-existent. Nevertheless, the chapter gives a nice overview of all meta-analyses that have been carried out. Chapter 12 exemplifies a case of applied studies with probiotics towards reducing mycotoxin amounts in food (although the title does not suggest this focus). The chapter culminates in a proof-of-concept example without reference to claims, and seems out of place in this book. Chapter 13 deals with paediatric probiotic research. The chapter lists the available evidence on allergic and gastroenteric disorders, but fails to define important aspects with respect to claim substantiation, which must be difficult to get in children, due to (more) ethical limitations. Perspectives with respect to claims related to over-the-counter (OTC) products and pharmaceutical preparations are discussed in Chapter 14. The current state of clinical evidence is evaluated so as to determine which claims are justified with regards to these products. It should be noted that these should be considered drugs rather than foods, and therefore an even more strict regulation applies.

Probiotics in the feed industry

Only a single chapter, Chapter 15, deals with probiotics in feed. In this chapter the authors have had to summarise all aspects that have been dealt with in all the other chapters

on human claims. It goes without saying that the authors had to be brief on each individual subject. It would therefore have been good to have an extended account on probiotics for feed in the book. Chapter 15 is well written and lists 25 probiotic products registered as feed additives in the European Union (list is not exhaustive). Unlike human probiotics, feed probiotics include many strains of *Saccharomyces*, *Bacillus*, *Enterococcus* and *Pediococcus*. Also unlike human probiotics, the evidence for efficacy of feed probiotics is usually greater. The authorisation processes are described, and three different institutions are involved in these: the EFSA to assess the dossier; the Community Reference Laboratory for Additives for Use in Animal Nutrition that assists the EFSA in scientific evaluation of the technical dossier, and the European Commission, which should authorise the evaluation of the EFSA. Efficacy has to be shown on the strain level (not different from human probiotics) and for every sub-category of the eight major animals categories where applicable (also not different for humans where data should be provided on the target population). There are a total of 31 sub-categories. At least 3 trials with a significant improvement have to be presented for each sub-category. This specific requirement does not exist for human dossiers.

Hurdles for product development

The last 4 chapters of the book describe case studies and barriers to probiotic product development from different angles. Chapter 16 describes the path of developing a multispecies probiotic combination targeted for non-infectious functional intestinal discomfort. The rationale behind the development of the product is given, and also the reasoning behind the choice of trials conducted. It gives a good account on how to build a scientific dossier. Whether or not it is sufficient to actually get a claim remains to be seen, because as far as I know, the dossier has not yet been evaluated by EFSA. The next chapter describes the hurdles experienced by small and medium-size enterprises (SMEs) in providing EFSA with dossiers that are sufficient for claim approval. Given the increase in R&D resources required for carrying out (multiple) clinical trials (or animal trials for that matter) necessary to substantiate a claim, the regulations should be considered a very difficult challenge for SMEs due to their often limited R&D budgets. The choices are developing a proprietary strain or using a strain from a larger probiotic company. Either way, the investment is usually substantial. A successful case study by an SME on the development of two bifidobacterial probiotics is given. General aspects on how to meet the criteria and requirements for claim approval are given in Chapter 18. Although several of these aspects have been dealt with in other chapters, the author describes in the future perspective section that at present approximately 30 strains can be classified as probiotics 'according to more-or-less proven beneficial effects'. Unfortunately the exact strains are

not given. But I wonder what the list would look like if the strains with 'more-or-less proven effects' were left out and only those with actual proven effects remained ... A helpful chapter is Chapter 19 on barriers to new applications for claims. The chapter addresses some of the negative opinions from EFSA and (potential) reasons why those dossiers did not succeed. Without being exhaustive, examples include the fact that in multispecies probiotics not all strains could be sufficiently characterised, or the mechanism of action of the product (or separate species) was unclear. This chapter is a must for those that are putting together a dossier, to see what has been considered important (and missing) in past dossiers. The last chapter deals with probiotics and innovation from an industrial perspective. It is a nice chapter, outlining that not all probiotics are the same from a genomic or functional perspective, nor in their capacity for cross-talking with the host. The authors postulate that innovative research helps in deciphering why and how probiotic strains differ. In their view innovation requires a capacity to detect early finding outside the norm, as well as confirmation of the robustness of these early findings. These

require expensive trials. On the other hand, companies depend on sales, and 'those who will benefit most from probiotics may not be able to offer the costs of sophisticated science.' Thus the challenge is to do the necessary amount of well-conducted science to be able to put together a dossier without the need for excessive and expensive demands from the regulatory bodies. It is unclear yet whether this balance will tip in favour of product development that is affordable to the consumers in need of probiotics that are actually proven to be functional.

Conclusion

In conclusion, I consider this book to be a must-have for all those evaluating their favourite strains with respect to claim substantiation. As intended by the editors, it allows for a comparison of health claims systems in different regions of the world. It contains helpful remarks with respect to putting together a dossier and is therefore imperative in your library of probiotic reference books.