Probiotics
From patent to consumer product
- a dairy case -

March - August 2011

HBO-Upgrade 12 ects.

Course: MST 80912

Student:
Hilde Boschloo
850312-107-060
hilde.boschloo@wur.nl

Supervisors:
Prof. Dr. S.W.F. Omta
Management Department
Wageningen University

Prof. Dr. S. Bröring
Food Chain Management
Hochschule Osnabrück
Management Department
Wageningen University

Preface

This report presents the final product of my HBO-upgrade. In my case this report is the last missing piece before I am able to graduate for the master 'Management, Innovation and Life Science'. During my master I have been studying different kind of aspects around management and life science, and in particular agricultural business economics. When I was searching for an interesting topic for this final assignment the idea came up to focus more on the 'innovation' part of my master. During my master I have studied innovation processes but with the main focus on human reaction to changes in their private or work environment. The feeling rises that it would be nice to study a case where innovation (or a part of innovation) was more business and industry orientated. This idea has resulted in the present project about probiotics. During the past months I have struggled with, for me, the totally new world of probiotic products, bacteria strains and patents. It took quite some time to get into the topic and find the right direction in the subject.

Hereby I would like to thank Prof. Dr. S.W.F. Omta and Prof. Dr. S. Bröring for helping me with the subject and giving me good advises on how this assignment should be executed and constructed.

Also I would like to thank my family, friends and boyfriend to stimulate me to continue working on the project also when the sun was shining.

Hilde Boschloo

August 2011

Content

List of tables

List of figures

List of abbreviations

ATCC	American Type Culture Collection
CDRD	California Dairy Research Foundation
CNCM	National Collection of Micro organism Culture
NCCAM	National center for complementary and alternative medicine
NCSU	North Carolina State University
NFF	Nutraceuticals and Functional Foods
PD	Product Development
R&D	Research and Development
Subsp	subspecies
USPTO	United States Patent and Trademark Office
WIPO	World Intellectuals property organisation

Introduction

Probiotics

Probiotics are an increasingly used additive in consumer products. Especially in the food industry the development of probiotic additives has led to many new hybrid consumer products on the shelf in supermarkets. The term 'probiotics' initially is an antonym from 'antibiotics'. Metchnikoff (1845-1916) was the first who developed a theory that senility is due to poisoning of the body by the products of certain bacteria. To prevent the multiplication of these bacteria he proposed a diet containing fermented milk. Metchnikoff advocated that soured milk containing bacteria may have positive effects on intestinal health. The majority of earlier research was on organisms that were used to produce fermented milk products such as yoghurt (Nobel Media AB, 2011; Ziemer and Gibson, 1998). The first use of real probiotic additives can be traced back to Kollath in 1953. Kollath described the restoration of the health of malnourished patients by different organic and inorganic supplements (Kollath, 1953, as cited in Vasiljevic and Shah, 2008). Ever since, a lot of research has been conducted on probiotics. Whereas every researcher used his own definition of probiotics, many different definitions will come across when searching for one. Therefore the FAO/WHO recommended in 2002 to define probiotics as 'live micro organisms that when administered in adequate amounts confer a health benefit on the host' (FAO/WHO, 2002).

Functional foods

The primary role of diet is to provide sufficient nutrients to meet the nutritional requirements of an individual. Today, probiotics are a popular additive to consumer products. Products which contain probiotics are part of a wide range of products which are called 'functional foods'. Functional foods were introduced long ago by Hippocrates with the motto 'Let food be your medicine' (Vasiljevic and Shah, 2008). Nowadays, there is increasing scientific evidence to support the hypothesis that some foods and food components have beneficial physiological and psychological effects over and above the provision of the basic nutrients. Those foods and food components can be taken to supplement to the primary food intake. Examples of functional foods include food that contain specific minerals, vitamins, fatty acids or dietary fibre, foods with added biologically active substances such as phytochemicals or other antioxidants and probiotics (EUFIC, 2006).

Converging industries

Whereas today probiotics are mostly known as an active ingredient to fortify dairy products, new industries that enter the probiotic market can be recognised. For example, the pharmaceutical industry is nowadays competing against the food industry in the area of nutraceuticals and functional foods (Bröring, 2010; Curran and Leker, 2011). When different industries use slightly the same techniques or knowledge, it can be described as converging industries. Converging industries are described by Choi and Valikangas (2001) as industries who show blurred boundaries by converging value proposition, technologies, and markets. The word 'converge' on itself is described as - come together from different directions so as eventually to meet - by the Oxford Dictionary (2011). Firms that find themselves in converging industries, face new competitors that produce substitute products for the same market (Bröring, 2010). From a management point of view it would be interesting to know how this industry convergence is playing a role in the product development and commercialisation of functional foods and new hybrid products. For stakeholders like investors, stockholder and managers information about the time and money involved in such development processes would be interesting for decision making matters. In this study some of the time issues around the development probiotics and the introduction of new products will be tackled.

Research objective

Problem description

The convergence between food and agriculture, pharmaceuticals, chemicals and even personal care have been recognised in recent studies (Bröring et al, 2006; Curran et al 2010; Curran and Leker, 2011). Prof. Dr. S. Bröring in close relation with Wageningen University is currently working on a broad research in field of probiotic products and the related industry convergence. Special interest in this field is the commercialization of new technologies emerging between two different industries; food and pharma. In figure I it is situated how the food and pharmaceutical industry are related.

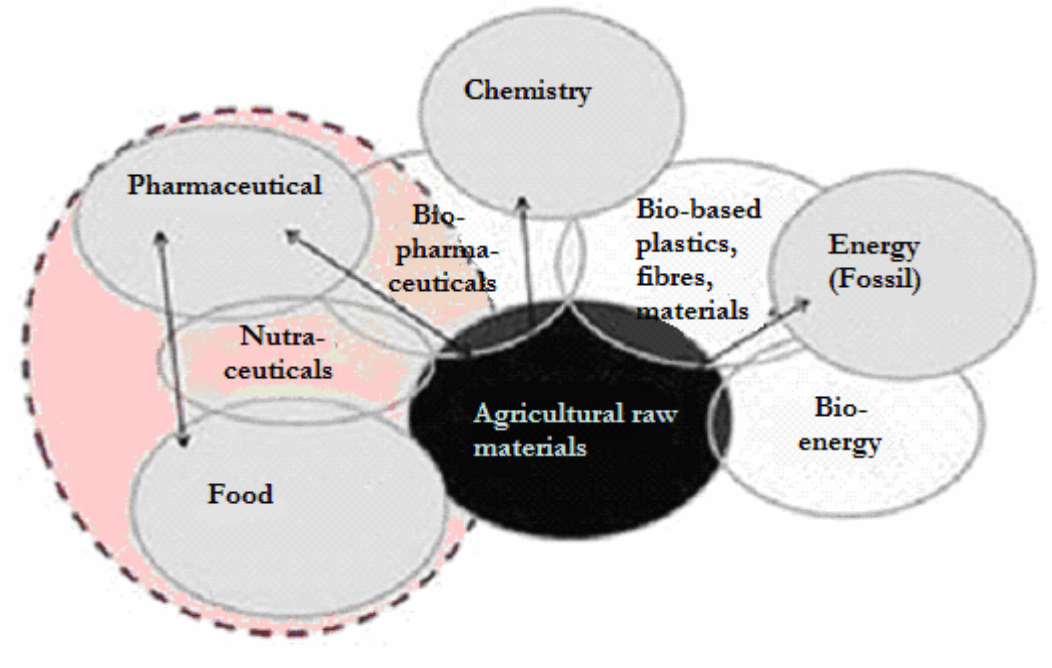


Figure I: Food - pharma industry convergence (source: Boehlje and Bröring, 2011)

Since 1981 there have been over 2000 patent applications on probiotics filed (with 'probiotics' mentioned in patent somewhere) and some 524 granted (in the USA and Europe) (Siezen and Wilson (2010). It can be presumed that these numbers are already higher right now. Although industry convergence can be recognised by analysing publicly available data, like scientific and patent references, as shown in research of Curran *et al* (2010), this still gives limited information about the final commercialization of probiotic products and the involved industries. This makes it difficult to detect whether knowledge and technology convergence lead to the industry convergence and finally to new products and/or new markets. Therefore the aim of this study is to detect whether industry convergence can be analysed in the process of product development

towards a commercialisation of new technologies. Hereby the probiotic field will be analysed from the back end. Some commercialized dairy products containing probiotic bacteria strains will be analysed to investigate the development process from patent to final product.

Objective

The objective of this study is to investigate the development of a selected group of bacteria strains used in commercialized probiotic dairy products by analysing patent and product information.

Sub-questions:

- What time does it take from patent to final commercialized product?
- What industries are involved in the development of the selected bacteria strains?
- Which industry finally brings the product to the market?
- Can technology convergence be recognised in the development process?
- Can industry convergence be recognised in the development process?

Literature review

Convergence over time

When searching for a good definition of converging industries many slightly similar descriptions can be found. Bezzina and Sanches (2005) describe convergence as the merging of separate fields. Lei (2000) describes that technological convergence occurs when advances or innovations commercialized in one industry begin significantly to influence or change the nature of product development, competition, and value-creating processes in other industries. Converging industries are described by Choi and Valikangas (2001) as industries who show blurred boundaries between industries by converging value proposition, technologies, and markets.

From a research point of view, Weaver (2007) characterizes the interest in industry convergence from an academic management perspective as marginal. Also Lind (2005) argues that academic literature is dealing with industry dynamics, industry structure, restructuring, market definitions and technological changes, but seldom explicitly mentions the term convergence. For years the electronics industry has been the only, most typical, example of technology convergence which is extensively described in literature. Technological convergence in industries like office equipment, computers, telecommunication, and consumer electronics has been so profound that in the 1980s many observers predict that they would soon merge into a unique sector, and that the main players in each of them would compete with each other. Gambardella and Torrisi concluded in 1998 that this trend towards a common electronics market has not been completed. It can be concluded that the merge into a unique sector takes more time than predicted. Although industries integrate technologies from other industries into their products, it can be presumed that the development of industry specific technologies still result in products which interests the consumer. Therefore it can be presumed that industry convergence in office equipment, computers, telecommunication, and consumer electronics can better be described as an ongoing process rather than a process which lead to one unique sector.

More recently, industry convergence has been recognised between the pharmaceutical and food industry. Even relative new terms can be recognised as a result of convergence. For example; the term 'nutraceuticals' describes the convergence between nutrition (food industry) and the pharmaceutical industry (Bröring and Leker 2007). Convergence has resulted in a new sector of nutraceuticals and functional foods (NFF). Whereas NFF can have multiple applications this research will mainly focus on the area of probiotics. It can be concluded that mainly four different industries can be recognized who show interest in the probiotics namely; chemicals, food & agriculture, pharmaceuticals and cosmetics & personal care (Walsh and

Lodorfos, 2002; Bröring *et al*, 2006; Krutmann, 2009; Curran and Leker, 2011). Walsh and Lodorfors (2002) describe Unilever as a good example of a firm which can be classified to the food industry, but also in the chemical-related business of making household and personal cleaning materials. In 2008 Unilever launched a probiotic containing ice-cream specially developed for kids (van der Meer, 2008). This perfectly indicates how specialised and complex the industry becomes whereby knowledge of food, pharma and nice markets (products especially for kids) result in a commercialised product. Walsh and Lodorfors (2002) describes that chemical and related product industries has reinvented itself as, firstly a life science industry and a more traditional chemicals and materials industry, and then by a further division of the life science industry into agro-food and pharmaceuticals. Boundaries between firms became blurred both by integration within common ownership structures and by the use of common technologies for production and new product search. Hereafter, a new separation of activities and identities took place, via a series of divestments and demergers separating distinct businesses, followed by a new round of consolidation by merger and acquisition, but this time among firms with similar product ranges (Walsh and Lodorfors, 2002).

Drivers of convergence

According to Katz (1996) one can identify three classes of drivers of convergence namely; technology change; evolution of business thinking; and evolution of regulatory thinking. Bröring (2010) describes that in the convergence in the food and pharmaceutical industries are mainly caused by the use of similar technologies and stimulated by the trend of regulatory convergence with respect to product approval (due to costly pharmaceutical-type clinical studies which are required in the approval for health claims).

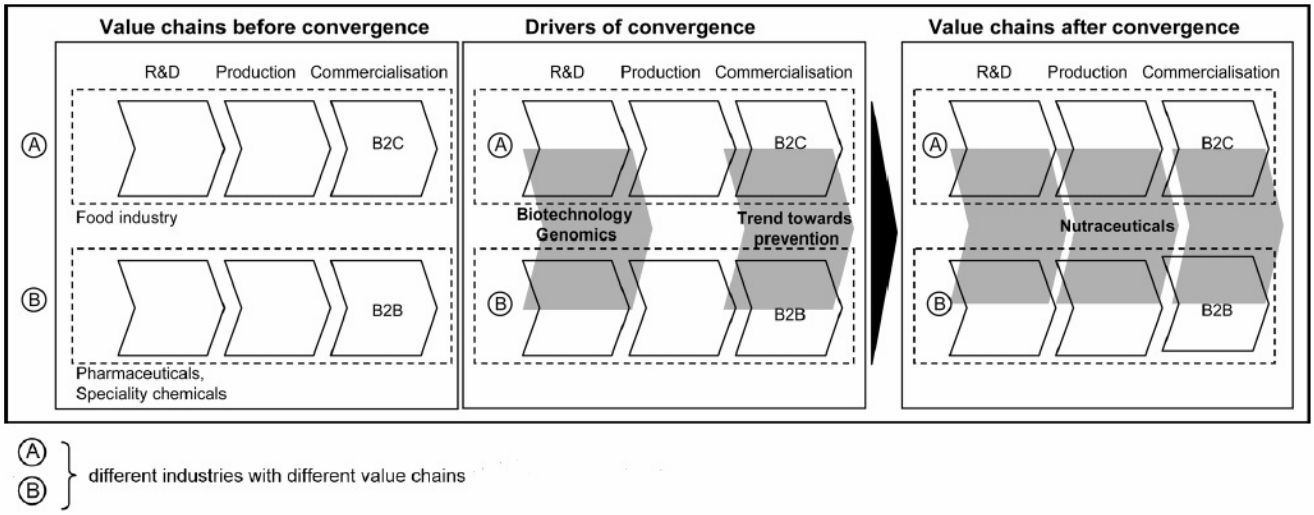


Figure II: Convergence of nutrition and pharmaceuticals: NFF sector (Bröring, 2010).

The pattern of industry convergence from Bröring (2010), presented in figure II, follows the work of Malhorta and Guota (2001). It presents that industry convergence is a result of both input-side and output-side convergence which leads to industry convergence. Input-side convergence is described as converging trends of technologies and technology-platforms. It is often induced by the development of new technologies which in turn leads to the development of a common technology platform. (Pennings and Puranam (2001) cited in Bröring and Leker, 2007). Output-side convergence is triggered by converging demand structures of different industries. This occurs when customers treat products of different industries in the same way. Products which originally where not in any competition start to become substitutes (Malhorta & Gupta, 2001 cited in Bröring and Leker 2007). Examples of such market-driven convergence are personal computers and televisions. Whereas in the beginning those products could be identified as different products, both products are increasingly being used as substitutes. Nowadays, personal computers have to possibility to play DVD's or even watch TV programmes (Bröring and Leker, 2007).

Types of convergence

Curran and Leker (2010) describe the different types of convergence. In figure III it is presented how the process of convergence will finally lead to industry convergence. Curran and Leker (2010) describe that the dashed lines indicate facultative dependencies, whereas solid lines represent obligatory connections between individual sequences. It can be seen that different types of convergence can be recognised during the process towards industry convergence.

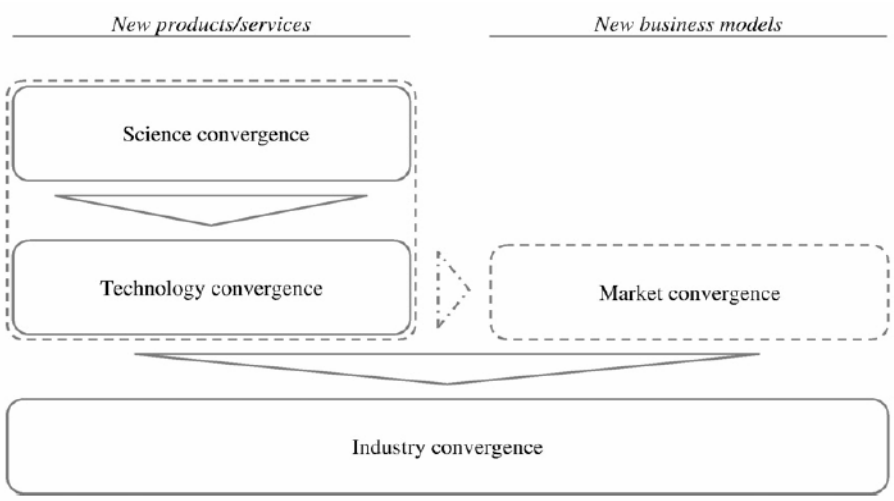


Figure III: Sequential process of industry convergence (Curran and Leker, 2010)

Figure III basically explains that industries with different scientific disciplines or areas converge into technology convergence whereby similar technology is used for different application areas.

This technology convergence may lead to market convergence whereby the demand from originally different markets starts to merge. Nevertheless it is possible that market convergence develops separately from the technology convergence. Finally technology convergence and market convergence will lead to industry convergence whereby the boundaries of industry starts blurring (Curran and Leker, 2010). This process has previously been described as input-side and output-side drives of industry converge.

The terms industry convergence and industry fusion have been used interchangeably in most cases. Nevertheless, there is as considerable difference. Curran and Leker (2011) describe *convergence* as a process, where objects move or stretch farther from their prior and discrete spots, to a new and common place. In contrast; *fusion* is described as a process where objects begin to merge with each other in the very same place of at least one of the objects. Curran and Leker (2011) describe that NFF can be interpreted as an example of convergence, as they are replacing neither the demand for nutrition nor the demand for full-scale medication. Smartphones is given as an example of fusion product of cameras, cellular phones, and portable computers.

Within convergence again different segments can be recognised. Greenstein and Khanna (1997) (citied in Kaluza *et al.*, 1998), debate that there are actually two primary kinds of convergence namely; convergence in substitutes and convergence in complements. They describe that two products converge in substitutes when customers consider two products to be interchangeable with each other. Convergence in complements can be the case when two products work better and more efficient together than separately. This occurs when companies develop standardized products or systems that interact to form a larger system. Bröring (2005) (cited in Curran *et al* 2010) describes similar theory where a new industry segment will either replace the former segments or will complement them at their intersection, i.e. leading to the formation of either a substitutive (1+1=1) new inter-industry segment or to a complementary (1+1=3) one.

Managing convergence

Innovation managers need to evaluate carefully whether the industry they are operating in may be affected by trends of convergence which calls for an effective monitoring of external developments not only inside their industry but also across industry boundaries, as critical knowledge may be developed in other fields (Bröring and Leker 2007). According to Lei (2000) convergence may lead to competitive conditions in which one industry's products or services are increasingly linked, absorbed, or blended with another industry's expanded range of offerings. Convergence leads to steady erosion of once-distinct boundaries among industries as they begin to share more similar competitive, market-based, and technological characteristics. Mark-Herbert

(2004) analysed Swedish food companies and concludes that competitive pressures, low prices and large volumes may not suffice as strategic advantage in the long-term. One way of gaining competitive advantage requires finding new ways of creating added value based on technology development.

When the first dairy product containing probiotics was commercialised this could be seen as an innovation. A definition of innovation given by Kotler and Keller (2006) is; any good, service, or idea that is perceived by someone as new. The growing demand for 'healthy' foods is stimulating innovation and new product development in the food industry internationally. Also the term 'disruptive innovation' can be used to describe the first launch of probiotic products. Disruptive innovation can be described as a totally new product in the market from which consumers demand has not been satisfied, or the demand was not even created. With respect to functional foods containing probiotics, it can be concluded that this segment nowadays is well established in the European market. Probiotic strains can be successful manufactured and incorporated into highly acceptable food products where they can retain their viability and functionality (Saarela, et al., 2000). The industry convergence plays an important role in the development of new markets and industry segments. Lei (2000) argues that as industries become closer, firms need to learn and invest in new types or core competences that allow them to deploy value-creating skills and core product platforms which can be easily reconfigured and adapted to a wider base of consumers across different markets. Hereby it is important to understand consumers and the innovation diffusion process around it.

Rogers (cited in Kotler and Keller, 2006) was the first who described this diffusion process in 1983. Rogers defines the innovation diffusion process as 'the spread of a new idea from it source of invention or creation to its ultimate users or adopters'. In figure IV it can be seen that the total adoption process of a new product takes some time.

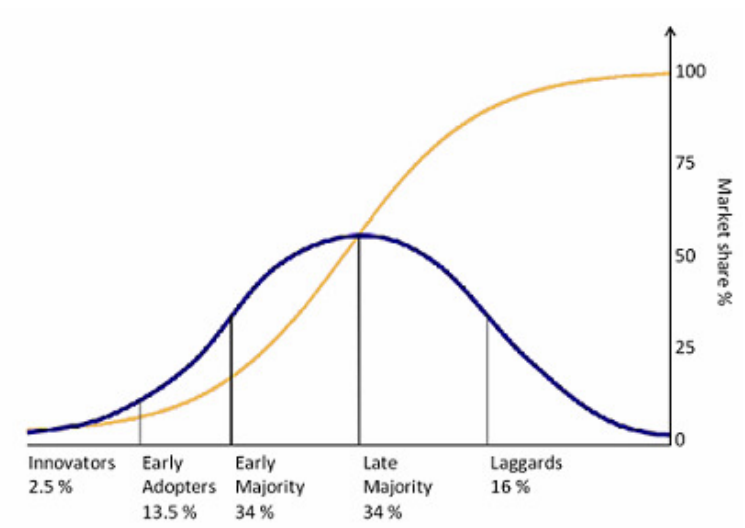


Figure IV: Time of adoption of innovation (source: Kotler and Keller, 2006)

Consumers who try new products which are launched on the market can be describes as 'innovators'. Those innovators only contribute for 2,5% to the total consumers who finally may use the product. This indicates that the early commercial phase of a product is very important in terms of consumer adaptation and to analyse how consumers respond on the product. Adopters of new products have been observed to move through five stages:

1. Awareness - The consumer becomes aware of the innovation but lacks information about it
2. Interest - The consumer is stimulated to seek information about the innovation
3. Evaluation - The consumer considers whether to try the innovation
4. Trial - The consumer tries the innovation to improve his or her estimate of its value
5. Adoption - The consumer decides to make full and regular use of the innovation

(Kotler and Keller, 2006)

Product development (PD) can be described as complex. Complexity in PD projects due to product design, the development process, the development organization, the tools and technologies applied the requirements to be met, and other domains (Danilovic and Browning, 2007). Bröring (2010) argues that innovation management of NFF products seems to be a complex endeavour as it combines the complexities of both the consumer market (brands, retail, ect.) and technological developments. This also applies for the PD of probiotic products. Especially from a R&D point of view it takes major efforts and costs to commercialize a final product. Thereby the threat of other industries working on substitute products increases the competition between industries. Where the probiotic preparation in liquid forms (like dairy) has been the most common product, it can be seen that R&D has also resulted in solid probiotic preparations like powdered products, pills and animal feed. New developments have resulted in probiotics that are able to survive heat and pressure of manufacturing processed and the acidic stomach environment. These new probiotic strains also remain viable without refrigeration, making new application possible. Think about cereal bars, biscuits, breads and cereal formulation. (Yamaguishi et al, 2011). Such developments are one way to create new markets within the existing probiotic market. Not only is the development of new strains a way to strengthen a business position in competition. It can be seen that in some cases different companies create a joint venture to be able to create the greatest market share in a country and in such way strengthen their competition position. A good example in the probiotic industry is the joint venture between Yakult and Danone. The joint venture was formed in 2005 to manufacture and sell probiotic drink Yakult in India and Vietnam. Whereas both Danone and Yakult had not been

present in Indian and the Vietnamese market, they agreed to work together on the consumer awareness of probiotic food towards a wider consumer acceptance Yakult 2011a; Yakult 2011e. From a disruptive innovation point of view it can be concluded that Yakult and Danone have worked together to develop a demand for probiotic diary products, products not known in India and Vietnam at that time. Such an agreement can be analysed as synergy. Schermerhorn (2008) described synergy as the creation of a whole greater than the sum of its individual parts. Synergy pools individual talents and efforts to create extraordinary results. Introducing new products to the market is one aspect of the complex PD process around NFF. It can be presumed that this synergy has made it possible to pool business competences like for example financial resources, knowledge of the culture, and creative marketing into one big campaign to promote probiotics. In this way Yakult and Danone have strengthen their competences to create a solid consumer market in which they could both be active.

Methodology

In the figure V the different stages of the present study have been made visible.

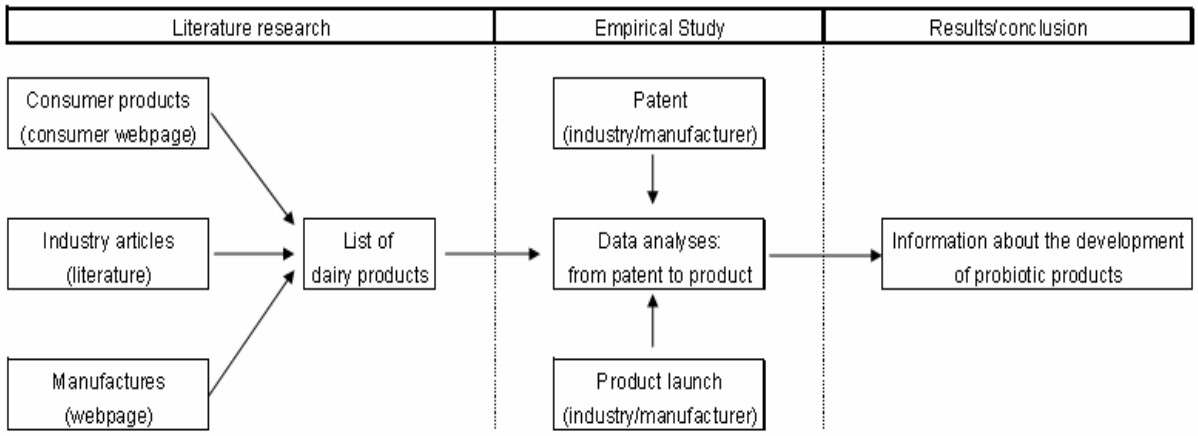


Figure V: Project overview

The aim of this study is to detect whether or not industry convergence can be analysed in the process of product development towards commercialisation of new technologies. Hereby a back end research strategy will be used to investigate the process wherein new knowledge reaches the commercial market. This will be done in the following steps:

- Definition of commercial probiotic product
- Definition of bacteria strain in the product
- Search for patent and patent owner of the particular bacteria
- Definition of industry background of the commercialised bacteria strain

Hereby the following information is tried to be found.

- When is the product launched on the consumer market?
- When is the particular bacteria strain in the product patented?
- Which manufacturer/industry patented the bacteria stain of the product?
- Which manufacturer/industry commercialized the probiotic product?
- What industry is behind the publication?
- Is the bacteria strain applied in other industries?

Literature research/ data collection

The main goal of the literature research is to create a structured list of probiotic products including the particular bacteria strains which are currently on the consumer market. This list will mainly be created based on the list which is published in the report 'Global Probiotics Market' by Marketsandmarkets in 2010. Next to this report Siezen and Wilson (2010) have created a list of examples of probiotic strains and product which will be included in this investigation. Additional information about the industry behind the product and manufactures will be obtained from consumer websites and academic articles (for example the website of NutraIngredients). Also consumer websites about dairy and health products will be used for finding new products and bacteria strains which are not included in the Global Probiotics Market report.

Patents

Information on patents of bacteria strains will be obtained from several patent databases like the European Patent Office (espacenet), the United States Patent and Trademark Office (USPTO), World Intellectual property organisation (WIPO) and Patentscope (part of WIPO). Additional information about certain bacteria strains will try to be found using the scientific database Scopus and OvidSP. To find extra information about patents Google Patent Search is sometimes used as a start. In particular when patents have to be found which are already expired (older than 20 years) it is sometimes difficult to find the first patent on a particular strain.

Data analysis and results

When reasonable amount of data is collected, data will be analysed on different aspects like: patent dates, product launch dates and industry types.

Bacteria strains

Commercialized bacteria strains

There are many bacteria strains which can be used in functional foods. Whereas a probiotic is a living microbial feed supplement, those bacteria should meet some standards to be useful as a functional food. The three main aspects are:

- The micro-organisms (bacteria) are alive
- The bacteria are administered orally
- The bacteria should be capable of reaching the intestine alive, in order to have an influence on the microbial balance (Food-Info, 2011)

The difficulty processing bacteria in food products is that they have to be resistant to influences they come across during their journey from manufacturing till their final destination, the intestine (Food-info, 2011). The probiotic strain must reach the intestine in a viable form and in sufficient numbers. This requires the survival of the probiotic during feed processing, including pelleting by heat in many application, it stability in feed storage over weeks and finally its safe passage through the adverse low pH conditions in the stomach (Simon, 2005). Due to this criterion the number of bacterial species and strains which can be used in functional food for humans are: Lactobacillus, Streptococcus and Bifidobacterium species. Those three genera are part of the lactic acid bacteria and are naturally present in the intestine as well as in many fermented (mainly acid) dairy products (Food-Info, 2011).

The following information is found on the website usprobiotics.org which is a non-profit research and education website made possible by the California Dairy Research Foundation (CDRF) and Dairy & Food Culture Technologies (2007). It presents a list of commercial strains currently sold as probiotics. Species are listed as reported by the manufacturer, which may not reflect the most current taxonomy. Note that to legitimately be called a "probiotic," strains must have undergone controlled evaluation for efficacy. The strains listed in this table may or may not have been adequately evaluated (CDRF, 2007). A quite similar list is given by MarketsandMarkets (2010) and Siezen and Wilson (2010).

Strain	Commercial products	Source
Lactobacillus acidophilus NCFM Bifidobacterium lactis HN019 (DR10) Lactobacillus rhamnosus HN001 (DR20)	Sold as ingredient	Danisco (Madison WI)
Saccharomyces cerevisiae (boulardii)	Florastor	Biocodex (Creswell OR)
Bifidobacterium infantis 35264	Align	Procter & Gamble (Mason OH)
Lactobacillus fermentum VRI003 (PCC)	Sold as ingredient	Probiomics (Eveleigh, Australia)

Lactobacillus rhamnosus R0011 Lactobacillus acidophilus R0052	Sold as ingredient	Institut Rosell (Montreal, Canada)
Lactobacillus acidophilus LA5 Lactobacillus paracasei CRL 431	Sold as ingredient	Chr. Hansen (Milwaukee WI)
Bifidobacterium lactis Bb-12	Sold as ingredient	Chr. Hansen (Milwaukee WI)
Lactobacillus caseï Shirota Bifidobacterium breve strain Yakult	Yakult	Yakult (Tokyo, Japan)
Lactobacillus caseï DN-114 001 ("L. casei Immunitas") Bifidobacterium animalis DN173 010 ("Bifidis regularis")	DanActive fermented milk Activia yogurt	Danone (Paris, France) Dannon (Tarrytown, NY)
Lactobacillus reuteri RC-14 Lactobacillus rhamnosus GR-1	Femdophilus	Chr. Hansens (Milwaukee WI) Urex Biotech (London, Ontario, Canada) Jarrow Formulas (Los Angeles, CA)
Lactobacillus johnsonii Lj-1 (same as NCC533 and formerly L. acidophilus La-1)	LC1	Nestlé (Lausanne, Switzerland)
Lactobacillus plantarum 299V	Sold as ingredient; Good Belly juice product;	Probi AB (Lund, Sweden); NextFoods (Boulder, Colorado)
Lactobacillus rhamnosus 271	Sold as ingredient	Probi AB (Lund, Sweden)
Lactobacillus reuteri ATCC 55730 ("Protectis")	BioGaia Probiotic chewable tablets or drops	Biogaia (Stockholm, Sweden)
Lactobacillus rhamnosus GG ("LGG")	Culturelle; Dannon Danimals	Valio Dairy (Helsinki, Finland) The Dannon Company (Tarrytown, NY)
Lactobacillus rhamnosus LB21 Lactococcus lactis L1A	Sold as ingredient	Essum AB (Umeå, Sweden)
Lactobacillus salivarius UCC118		University College (Cork, Ireland)
Bifidobacterium longum BB536	Sold as ingredient	Morinaga Milk Industry Co., Ltd. (Zama-City, Japan)
Lactobacillus acidophilus LB	Sold as ingredient	Lacteol Laboratory (Houdan, France)
Lactobacillus paracasei F19	Sold as ingredient	Medipharm (Des Moines, Iowa)
Lactobacillus paracasei 33 Lactobacillus rhamnosus GM-020 Lactobacillus paracasei GMNL-33	Sold as Ingredient	GenMont Biotech (Taiwan)
Lactobacillus plantarum OM	Sold as Ingredient	Bio-Energy Systems, Inc. (Kalispell, MT)
Bacillus coagulans BC30	Sustenex, Digestive Advantage and sold as ingredient	Ganeden Biotech Inc., Cleveland, Ohio
Streptococcus oralis KJ3 Streptococcus uberis KJ2 Streptococcus rattus JH145	ProBiora3 EvoraPlus	Oragenics Inc. (Alachua FL)
Lactobacillus rhamnosus PBO1 Lactobacillus gasseri EB01	EcoVag	Bifodan (Denmark), www.ecovag.com

Table I: Commercial strains sold as probiotics (CDRF, 2007; MarketsandMarkets, 2010; Siezen and Wilson 2010).

This study will investigate the development of several bacteria stains. Since limited time is available for this study, not every bacteria strain will be investigated. Therefore the main focus will be on bacteria strains which currently can be found in commercial dairy products. Hence, the commercial availability of the strains on the market serves as selection criterion. Accordingly, a new list is created which present some probiotic dairy products (see table II).

Name of the product	**Manufacturer**	**Bacteria strains**
Actimel	Danone	Lactobacillus Caseï DN-114001
Yoplus	Yoplait/General Mills	Bifidobacterium lactis Bb-12
Yoptimal	Yoplait/General Mills	Bifidobacterium lactis Bb-12 Lactobacillus acidophilus LA-5 Lactobacillus rhamnosus LGG
Stonyfield yoghurt	Stonyfield farm	
Yakult	Yakult Honsha	Lactobacillus Caseï Shirota

Table II: Examples of probiotic dairy products

Lactobacillus Caseï DN-114001

The bacteria strain Lactobacillus Caseï is one of the most studied bacteria species and has many applications. However, the particular bacteria strain Lactobacillus Caseï DN-114001 is mainly used in the dairy product Actimel from Danone.

Danone has a long history in research and PD in the probiotic field. Danone was set up by Isaac Carasso in Spain in 1919. Carasso was appalled by the intestinal disorders affecting children in Barcelona as a result of the poor hygiene and warm climate. Carasso had heard doctors talking about yogurt, a fermented milk product unknown in Spain. Around these days Elia Metchnikoff (at that time director of the Institute Pasteur in Paris) studies similar areas which encouraged Carasso to develop and launch yoghurt products in Spain (Danone Geschiedenis, 2010; Building Danone, 1996).

Patent

The strain Lactobacillus Caseï DN-114001 is described in The Patent Cooperation (PCT) application WO 96/020607 in the name of: Compagnie Gervais Danone, and was deposited on 30 Dec. 1994, with the CNCM (National Collection of Microorganism Culture) held by the Institute Pasteur, 25 rue du Docteur Roux, in Paris, under the number I-1518, claiming that beneficial properties in the context of treating diarrhoea has been shown.

Another product of Danone is Activia. Danone explains the differences between Actimel and Activia. Actimel contains the bacteria strain Lactobacillus caseï Defensis (DN-114001) which basically affects the upper part of the intestine and gives a positive health influence. Activia contains the bacteria strain Bifidus ActiRegularis (Bifidobacterium Animalis DN-173010, CNCM 1-2494) which has been isolated by Danone Vitapole researchers in 1985 (Actimel, 2011; Activia, 2011). This strain is sometimes designated as Bifidobacterium animalis and affects the lower part of large colon (Actimel, 2011). Activia has already launched to the market in 1987 under the name 'BIO' (Danone Research, 2008). It is not known whether this bacteria strain is used for other applications. Nevertheless, the strain is submitted to the time line (table III) whereas it gives useful information about the time it takes to develop useful bacteria strains and the time it takes to commercialise the bacteria strain in a dairy product.

Product overview

Danone (the producing manufacturer) claims that the first launch of Actimel was in 1996 in Spain (Danone, 2011). In another publication of Danone Reserach it can be read that the launch was in 1994 (Danone Research, 2008). From this it can be presumed that Danone Research started working with the product in 1994 and that the final product launch to the market was in 1996. In the United States and Canada the product is known as DanActive. Ever since, Actimel has grown continuously. One of the keys to this success was the decision in 2001 to adapt Actimel's sales argumentation to each consumer group. This resulted in TV advertising that featured a mother with her children, professional adults and, finally, seniors. Each advertising spot highlighted specific benefits for each consumer group. For example, mothers where reminded how Actimel helps reinforce children's natural defence mechanism and seniors how Actimel helps to provide protection.

Globally, Actimel is present in more than 30 countries, has also been growing fast - 12% in 2006 - and sales have reached €1 billion. As in Spain, product's health positioning is focussed on its ability to strengthen the body's natural defences (Belbe, 2009)

In 2005 The Institute Pasteur and Danone Research have started a partnership agreement to conduct joint research in the field of probiotics, for an initial period of 4 years (Danone Research, 2008). The Institute Pasteur is a private non-profit foundation which contributes to the prevention and treatment of disease, through research, education, and public health activities (Institute Pasteur, 2011). In 2008 this has resulted in a new patent with publication No. EP 1838158 B1 on 16 July 2008. This patent enters a slightly new area whereby the probiotic strain DN-114001 is been used for the prevention or treatment of a delayed-type hypersensitivity reaction (commonly known as eczema).

Time line of Lactobacillus Caseï DN-114001

Year	Type	Content	Effect	Industry application	Industry background of the company
1985	Bacteria	Isolation of Bifidobacterium Animalis DN-173010	Research	Dairy	Danone --> Food company
1987	Product launch	BIO' with Bifidobacterium Animalis DN-173010	Intestine	Dairy	Danone --> Food company
1994	Patent	Deposit Danone Lactobacillus Caseï DN-114001	Intestine	Dairy	Danone --> Food company
1996	Product launch	DanActive in America	Intestine	Dairy	Danone --> Food company

Year	Type	Content	Effect	Industry application	Industry background of the company
2005	Partnership	Joint research in probiotics between Danone and The Pasteur Institute	Research	Dairy/Medical	Food and Diseases
2008	Patent	Lactobacillus Caseï DN-114001 to prevent/treatment of eczema	Skin	Dairy	Danone and The Pasteur Institute --> Food and Disease treatment

Table III: Time Line Lactobacillus Caseï DN-114001

Conclusion

It can be concluded the bacteria strain Lactobacillus Caseï DN-114001 at this moment is only used in dairy products which claims to boost the immune system. Due to the joint research with The Pasteur Institute it can also be concluded that not only the food industry show interest in this bacteria strain, but also research institutes which contributed to the prevention and treatment of diseases. This joint research has resulted in new knowledge and patent in a new area of eczema treatment. It is not known whether this patent has resulted in a commercialized product. Nevertheless, this shows how different industries can combine their knowledge and find new application areas for the existing bacteria strain. This process can be analysed as an early stage of industry convergence. When looking at the different types of convergence (presented in figure III) and compare those with this case of joint research into Lactobacillus Caseï DN-114001, it can be best analysed as technology convergence, which might finally result in industry convergence.

Bifidobacterium lactis Bb-12

The Bifidobacterium lactis Bb-12 is a bacteria strain which is manufactured by Christian Hansen. This bacteria strain can be found in the dairy product Yoplus from Yoplait. The bacteria stain is also known under the code CNCM I-3446.

Patent

Bifidobacterium was first isolated by Henry Tissier (of the Institute Pasteur) in 1899 from a breast-fed infant, and he named the bacterium Bacillus bifidus communis. Tissier claimed that bifidobacteria would displace the proteolytic bacteria that cause diarrhoea and recommended the administration of bifidobacteria to infants suffering from this symptom (World Gastroenterology Organisation, 2008). Ever since, many strains of Bifidobacterium have been discovered, researched and patented and used for commercial products.

The bacteria strain Bifidobacterium lactic (CNCM I-3446) is sold by the Christian Hansen company of Denmark in food products since 1985 (Hansen CHR, 2011a; Szajewska, 2010). The trademark for the strain Bb-12 is obtained at 13 August 1999.

In the study of Masco *et al* 2004 the bacteria strain in debated as follows. 'The taxonomic standing of the species Bifidobacterium lactis has been much debated and several studies have investigated its affiliation with the closely related but earlier described Bifidobacterium animalis. Based on phenotypic characteristics, Cai *et al.* (2000) proposed that Bifidobacterium lactis should be considered as a junior synonym of Bifidobacterium animalis. However, new genotypic evidence, recently reported by Ventura & Zink (2002, 2003) and Zhu *et al.* (2003), suggested that Bifidobacterium lactis and Bifidobacterium animalis should still be considered to be two separate taxonomic entities, not at the species level but at the subspecies level' (cited in Masco *et al*, 2004).

At 12 October 2009 Nestec S.A. patented the strain for the application of infant formula with probiotic. The patent can be found with the number: 20090304655. Two years earlier, Nestle had introduced their new 'Good start Natural Cultures infant formula' which seems to contain the bacteria strain Lactobacillus Lactis Bb-12 (Sanders, 2007). Nevertheless, this product uses the trademark 'Bidido BL' which makes it difficult to conclude whether this product uses the Christian Hansen strain, or a close related sub-species.

Another application is patented by L'Oreal under patent number 7651680 which claims to found a methods and compositions for preventing and treating sensitive and dry skin (application date 26-01-2010, issued date 23-06-2005).

Products

Yoplus

The company General Mills launched Yoplus in the U.S. targeting woman for their digestive problems (regulate digestive health). In the US and Canada Yoplus launched in 2007 (Euromonitor International 2011, Yoplait, 2007a). In Canada the product is on the market with the name Yoptimal (Yoplait 2007b). The product claims to have a blend of Bifidobacterium lactis Bb-12, plus a specific type of fibre. The natural fibre in Yoplus is added as a prebiotic, a food ingredient that enhances the actions of probiotics. One serving of Yoplus provides three grams of inulin, a natural, non-digestible fibre from chicory root extract. Inulin serves as food for the probiotic in the digestive tract and selectively stimulates growth of Bifidobacteria. Therefore, Yoplus claims to provide a synbiotic relationship of the probiotic culture Bb-12 and the prebiotic inulin (Yoplait, 2007a; MarketandMarkets, 2010).

Whereas the bacteria strain Bb-12 is commercialised by Christian Hansen to sell as a food ingredient or feed supplement, it can be found in many products. In the time line the products Probitic of USANA and Yovis Regola from Sigma-tau Avant-garde Spa are presented as examples of products that currently make use of the Bb-12 and which are not dairy products (USANA, 2009; Hansen CHR, 2011b). At the website of Christian Hansen it can be found that those products have been developed in close collaboration with Christian Hansen (Hansen CHR, 2011a, Hansen CHR, 2011b). Whereas most products claim to give beneficial effect on intestine health, a new application area can be found. L'Oreal has patented an application which claims that the bacteria strain can help preventing and treating sensitive and dry skin.

Time line of Bifidobacterium lactis Bb-12

Year	Type	Content	Effect	Industry application	Industry background of the company
1985	Bacteria	Christian Hansen used CNCM I-3446 in food products	Intestine	Dairy	Christian Hansen --> health and nutrition
1999	Trademark	Bb-12 becomes trademark of Christian Hansen	Intestine	Dairy/supplement	Christian Hansen --> health and nutrition
2007	Product launch	Yoplus launch in US and Canada	Intestine	Dairy	General Mills --> dairy

Year	Type	Content	Effect	Industry application	Industry background of the company
2007	Trademark	Bifidus BL by Nestec			Nestec S.A. (Nestlé) --> Food company
2009	Patent	Nestec S.A infant formula with probiotics	Intestine Baby	Food supplement	Nestec S.A. (Nestlé) --> Food company
2009	Product launch	Probiotic' with Bb-12 and LGG	Intestine	Food supplement	USANA --> health and nutrition
2010	Patent	L'Oreal preventing and treating sensitive and dry skin	Skin	Feed supplement	L'Oreal --> Cosmetics
2011	Product launch	Yovis Regola containing Bb-12	Intestine	Feed supplement	Sigma-tau Avant-garde Spa --> Pharmaceutical

Table IV: Time Line Bifidobacterium lactic Bb-12

Conclusion

The bacteria strain Bifidobacterium lactic Bb-12 is just one strain which is closely related to the *Bifidobacterium animalis* subsp *animalis* and *Bifidobacterium animalis* subsp *lactis*. As mentioned before scientific and commercial names used on products can differ. When searching for patents, many can be found. Most patents claim to have found slightly different intestine effects in relation to the ones already existing. Those patents have not been included in the time line because they are not a result of new technology. It can be presumed that this strain is so much patented due to the fact that this strain can easily been purchased and used for research. Whereas most applications claim to give beneficial effects on the intestine, a more recent patent claims to give beneficial effects on the skin. The collaborations between Christian Hansen and companies like USANA and Sigma-tau Avant-garde Spa present how different industries work together which results in new products. Christian Hansen (2011b) describes that by combining the unique probiotic know-how of Christian Hansen with the commercial strengths of the Italian company Sigma-Tau has resulted the probiotic product 'Yovis Regola'. This kind of collaboration can be analysed as synergy whereby both companies combine their business competences which has resulted in a new product. Even collaborations between companies who originally had no common interest become visible. Good examples are the products of the Laboratoires Innéov. It can be presumed that Innéov is the result of the patent of L'oreal in 2010. Whereas in the patent the strain Bb-12 is one of the used bacteria strain, the final product contains other strains (this is why the products cannot be found in the time line). The product involves a feed supplement which includes probiotics and antioxidants and claims to affect the skin. The first probiotic products in this new

area have been launched in 2008. The products are developed by Nestlé and L'Oréal. On the website they even introduce a relative new term 'nutracosmetics' (Inneov, 2011; L'Oreal, 2004, Bird, 2009). The product line of Innéov is a joint venture which started in 2002 between L'Oreal and Nestlé. They argue that L'Oréal and Nestlé both have complementary state-of-the-art research material. The joint venture; laboratoires Innéov, was set up so that a growing consumer interest in skin and hair health could be satisfied, drawing on the best in both nutrition and cosmetic research (Nestlé, 2006).

Analysing this case it can be concluded that industry convergence can be recognised in the food, pharmaceutical and even in the cosmetic industry whereas these industries all have launched one or several products.

Lactobacillus acidophilus LA-5

The bacteria stain Lactobacillus acidophilus LA-5 can be found in many applications. The company Christian Hansen is selling this bacteria strain for commercial applications.

Patent

Lactobacillus acidophilus is a bacteria strain first described by Moro in 1900 which he named Bacilluc acidophilus. It is argued that it is possible that the organism described by Moro nowadays is known as Lactobacillus acidophilus. As a paediatrician, Moro has focussed his research mainly on intestinal problems and solutions for kid's health (Hansen and Mocqout, 1970; Weirich and Hoffman, year unkown).

One of the first patents which can be found, and which might indicate a prior stage of the today's Lactobacillis acidophilus LA-5, is about 'a method of culturing' (1982, 14 September, with filling 1978, 27 January from the assignee TransAgra Corporation in Memphis with patent number: 4349569. TransAgra objective of the research was to produce a Lactobacillus acidophilus strain more resistant to Lactic acid. When searching for information about TransAgra, useful information is lacking. Only some trademark registration can be found which indicated that TransAgra is mainly operating in the industry of veterinary supplements and pharmaceuticals (TradeMarkia, 2011). In 1983 a patent can be found which claims to have found a bacterial preparation for prophylaxis of intestinal disturbance, especially salmonella infections, in poultry containing multiple strains including Lactobacillus acidophilus (U.S. Patent 4689226).

The first patents about the probiotics use of Lactobacillus acidophilus for humans are dated at 13 June, 1989 and 16 July, 1991, (US patent 4839281 and 5032399) by Gorbach and Goldin. These patents indicate that the strain was isolated in North Carolina State University (NCSU). Studies have yielded evidence that the NCSU strains, when ingested by humans or animals, produce beneficial effects on various functions of the gastrointestinal tract.

Based on the website of Christian Hansen (2011c) Lactobacillus acidophilus is used since 1979 as an ingredient in food and dietary supplement. It can be presumed that the bacteria those days were mainly used as bacteria to ferment other products. Patent can be found in 1977 which claims to have found a 'starter culture media containing whey', which is in the description explained as a starter culture for cheese production (patent 4020185). Since 22 January 1997 Christian Hansen got the trademark over the Lactobacillus acidophilus LA-5 by U.S. federal trademark registration with serial number: 75229365 with the service of bacteriological preparation containing lactobacillus acidophilus in the diary industry.

Products

Lactobacillus acidophilus is often used but mainly in powdered products and pills. In dairy this strain can be found in Yoptimal from General Mills. Yoptimal has been launched to the market in 2007 and contains two probiotic bacteria strains namely Lactobacillus acidophilus LA-5 and Bifidobacterium lactic Bb-12 (Yoplait, 2007b). In collaboration with Christian Hansen, Sagitus has developed the product LIVEO which has been launched in 2007. The product contains both the bacteria Bb-12 and La-5 (Hansen CHR, 2011d). Besides the strain from Christian Hansen, some close related strains can be found in the market. Lactobacillus acidophilus DDS-1 is produced by Nebraska Cultures. This strain has been found in the late 1950's by Dr. Khem Shakani, founder of Nebraska Cultures, which nowadays presents themselves as leaders in probiotic technology (Nebraska Cultures, 2011). The strain DDS-1 can be found in many food supplements. Whereas most of these products claim to affect the intestine, new products can be found which claims to have beneficial effect on the skin. DermaEssential Skin Pack is a product manufactured by DermaHarmony which offers an approach to managing psoriasis and other chronic skin conditions (DermaHarmony, 2011). Unfortunately no product launch data can be found. Another strain (Lactobacillus acidophilus NCFM) is manufactured by Dansico. Dansico presents themselves as world leader in food ingredients, enzymes and bio-based solutions (Dansico, 2011a). The products from Dansico can both be used as starter cultures for the fermentation of food but also as probiotics to strengthen the immune system and reduce intestinal disorders (Dansico 2011b).

Time line of Lactobacillus acidophilus LA-5

Year	Type	Content	Effect	Industry application	Industry background of the company
1900	Discovery	Bacteria found called Bacilluc acidophilus	Intestinal kids	Medical	E. Moro --> Paediatricians
1977	Patent	Starter culture media containing whey	Milk fermentation	Dairy	Unknown
1978	Patent	a method of culturing acidophilus	Research	Unknown	TransAgra --> Pharmaceuticals and Veterinary supplements
1979	Product	Lactobacillus acidophilus strains used for food and dietary supplements	Milk fermentation	Dairy	Unknown
1983	Patent	Protect poultry against salmonella with processed mixture	Animal Intestine	Animal health	Farmos-Yhtyma --> Unknown

Year	Type	Content	Effect	Industry application	Industry background of the company
1989	Patent	Lactobacillus acidophilus strain method of selection	Research	Medical	Gorbach/Goldin --> Pharmaceutical
1991	Patent	Lactobacillus acidophilus strains	Research	Medical	Gorbach/Goldin --> Pharmaceutical
1997	Trademark	LA-5		Dairy and Supplements	Christian Hansen --> health and nutrition
2007	Product Launch	Yoplait including LA-5	Intestine	Dairy	Yoplait --> Food company
2007	Product Launch	LIVEO dietary supplement for adults and kids	Intestine	Supplement	Sagitus --> Pharmaceutical

Table V: Time Line Lactobacillus acidophilus LA-5

Conclusion

Many patents and products can be found which make use of the Lactobacillus acidophilus. In the time line it can be seen that multiple industries show interest in this bacteria strain. In 1900 the focus was mainly medical based. Over the years it can be seen that other industries have picked up the idea that lactobacillus acidophilus give beneficial effects to the intestine. This process can be described as technology convergence. Industry convergence can be analysed in the food and pharmaceutical industry whereas they have launched several products using the same technology. From a market based view it can be concluded that there are many products (mostly food supplements) on the market which all claim to have the same effects which result in high competition on the market.

Lactobacillus Caseï Shirota

The Lactobacillus Caseï Shirota is a bacteria strain used in products of Yakult.

Patent

In 1930 Dr. Shirota managed to isolate and cultivate lactobacillus that proved to be strong enough to survive the journey to the large intestine. This bacteria strain is known as Lactobacillus Caseï Shirota (Yakult, 2011b, Yakult, 2011c). Whereas records from patents during that time are not available in patent databases it is difficult to find a record about any patent of this strain. The first patent which has been found from Yakult is dated 10-7-1973 (issued date 1-11-1966, patent BRPI6684297). This patent however has no relation with the bacteria application in dairy products. The patent document is written in Portuguese and claims to have found a new model for plastic packaging of drinks. In 1968 Yakult replaced the original glass bottles with the foil capped plastic bottles (figure VI). Whereas the plastic bottles weighed less than the glass bottles, Yakult door to door sales forces were able to carry more bottles on their rounds (Hayes, 2011; Yakult, 2011b). Yakult produces all plastic bottles themselves to guarantee the best quality of the total product (Franke, 2011).

Figure VI: from glass towards plastic bottles.

In 1935 Shirota developed his first dairy product; Yakult, which contained high concentrate viable Lactobacillus Caseï Shirota. In the beginning Yakult was only introduced in Japan and Taiwan. In 1968 they start selling in Brazil, due to the large number of Japanese immigrants in the country. Nowadays Yakult is sold in many countries (Franke 2011 and Yakult, 2011b).

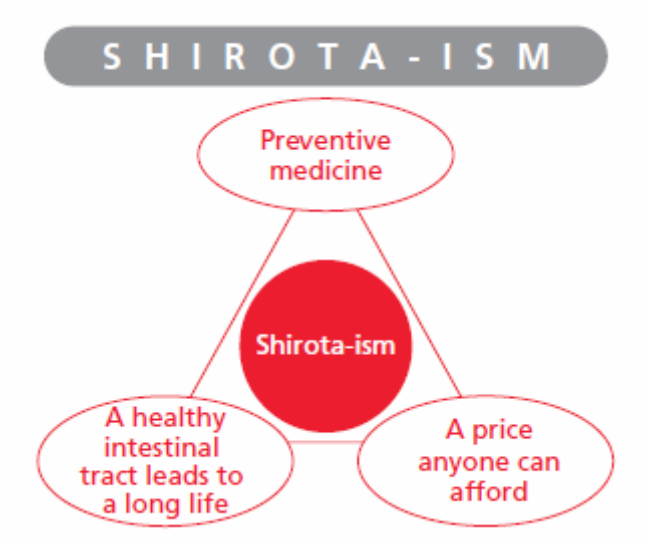


Figure VII: Shirota-ism -root of all business activities

Products

Yakult has launched several products containing the Lactobacillus Caseï Shirota strain. A product overview of dairy applications can be found in appendix I. Whereas the discovery of Lactobacillus Caseï Shirota had a medical background, Yakult was launched as a dairy product to a broad target group. This is due to the ideas of Dr. Shirota and referred as Shirota-ism (figure VII) and serve as the root of all Yakult's business activities (Yakult, 2011d). In 1938 Yakult was officially registered as a trademark. To expand the selling figures Yakult introduced the Yakult ladies in 1963. At this moment around 80.000 Yakult ladies can be found all over the world selling Yakult door-to-door. Besides selling Yakult those ladies have a social role in society and give health advises (Yakult, 2011b). The Yakult Ladies have stand on the beginning of the Yakult's cosmetic line. Whereas the glass bottles had to be cleaned they discovered that by applying this milk on their hands resulted in a very soft skin. This is where research into cosmetic applications at Yakult started. Yakult have launched several cosmetic products in 1971, but contain other types of bacteria which seem to be more beneficial for external skin use (Franke, 2011; Yakult 2011b). In 1975 and 1979, some medical applications containing the Lactobacillus Caseï Shirota have been launched to the medical and healthcare industry (Yakult, 2011b).

Time line of Lactobacillus Caseï Shirota

Year	Type	Content	Effect	Industry application	Industry background of the company
1930	Research	Dr. Shirota discovered the Shirota strain	Intestine	Research	Dr. Shirota →Medical
1935	Product launch	Yakult product launch in Japan	Intestine	Dairy	Yakult --> Health & Nutrition
1938	Trademark	Yakult was registered as a trademark			Yakult --> Health & Nutrition

Year	Type	Content	Effect	Industry application	Industry background of the company
1963	Research	Yakult ladies, first step towards a cosmetic line of Yakult	Research	Cosmetics	Yakult --> Health & Nutrition
1970	Product launch	Joie drinking yoghurt	Intestine	Dairy	Yakult --> Health & Nutrition
1975	Product launch	Biolactis Powder	Intestine	Pharmaceutical	Yakult --> Health & Nutrition
1979	Product launch	Yakult Seichoyaku intestinal regulator	Intestine	Pharmaceutical	Yakult --> Health & Nutrition

Table VI: Lactobacillus Caseï Shirota

Conclusion

The bacteria Lactobacillus Caseï Shirota is only used in products manufactures by the company Yakult. The time line shows how the development of the bacteria has resulted in different kind of products which are launch into different product markets. Whereas from origin the research was basically medical orientated, the first product can best be described as a dairy product intended for a broad customer group in Japan. Further research has resulted in more products in the dairy industry, but also in the pharmaceutical industry. This shows that the company is operating in different industries. Besides diary and pharmaceutical products, Yakult has resulted in new research where bacteria are used in cosmetic products. The cosmetic line which is launched by Yakult Company contains a different type of bacteria which is more suitable for application to the skin. Nevertheless, this shows the how knowledge can be the start of new research and finally results in product launches in markets of other industry. It can be concluded that this is an interesting example of technology convergence whereby technology is used to enter new markets.

Lactobacillus Rhamnosus

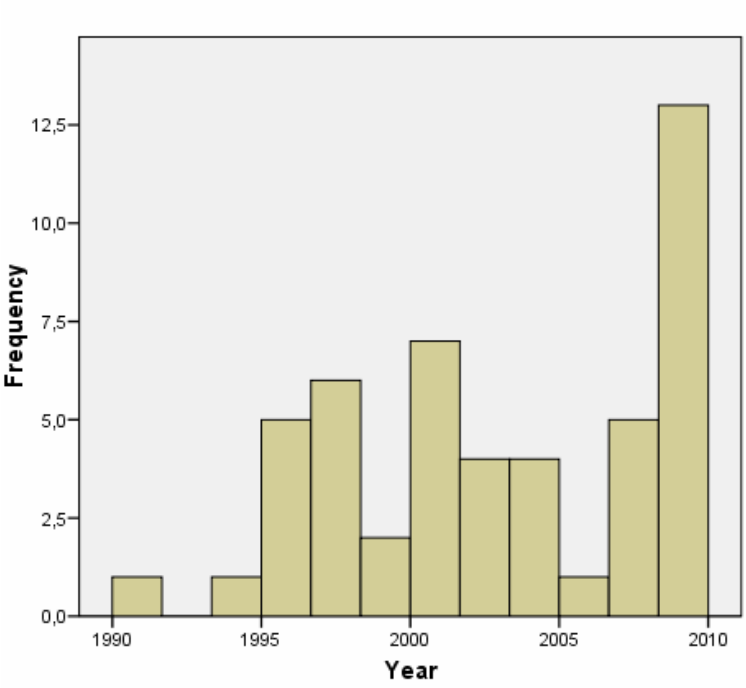
The bacteria strain Lactobacillus Rhamnosus is one of the most researched bacteria stains. Especially the Lactobacillus Rhamnosus GG is used over 25 countries (Food-info, 2011). Several applications can be found around this bacteria strain. Most often this bacteria strain is known as Lactobacillus Rhamnosus LGG. LGG is a trade mark from Valio (Finland) and got these exclusive rights in 1987. This was followed by research on the strain by Valio's R&D centre and many other research institutes. The product launch of Gefilus including LGG became reality in 1990 (Valio Ltd, 2011a).

Patent

One of the first patents found including the bacteria strain Lactobacillus Rhamnosus is found at 27 July 1988 (with an application date of 10 December 1987). This patent claims the preparation for the treatment of gastric disorders. According to the abstract of the patent, the invention relates to a preparation for use in the treatment of enteric disorders in animals including man, to a process for producing the composition and to a kit suitable for use in producing the composition (patent ZA1987/09287). The second patent on Lactobacillus Rhamnosus is published on 13 June, 1989 (issued date 17 april 1985) by Sherwood Gorbach and Barry Goldin. The GG derives from the first letters of their surnames. They claim to have found a biologically pure culture of bacteria of a Lactobacillus species in which the bacteria have avid adherence to intestinal cells, are able to survive at low pH, and produce large amounts of lactic acid, (US patent 4839281). The depositor of this strain is New England Medical Center Hospitals, Inc. From this it can be concluded that the first researches into this bacteria strain had medical background. In 1987 Valio has made a license agreement concluded with Gorbach and Goldin to use the strain under trade name Lactobacillus Rhamnosus LGG. Or today often only used as LGG (Valio Ltd, 2011b; Food and Functionals, 2011b).

Product overview

A lot of products can be found containing the LGG bacteria. Examples of these products can be found in Appendix II (Valio Ltd 2011c). In total 49 diary products have been launched to the market in the past years in different countries. A distribution of these launches can be found in the figure VIII. This only presents different years in which products are launched. This includes same products only with different launch years in other countries.



Year

		Frequency	Percent
Valid	1990	1	2,0
	1994	1	2,0
	1995	1	2,0
	1996	4	8,2
	1997	1	2,0
	1998	5	10,2
	1999	2	4,1
	2000	3	6,1
	2001	4	8,2
	2002	1	2,0
	2003	3	6,1
	2004	4	8,2
	2005	1	2,0
	2007	2	4,1
	2008	3	6,1
	2009	5	10,2
	2010	8	16,3
	Total	49	100,0

Figure VIII: LGG Dairy product launches in past years (figure based on data from Valio Ltc 2011c).

When analysing the different applications of the LGG bacteria it can be seen that LGG is applied to many types of products. In table VII examples of first product launches can be found. The table perfectly illustrates how different industries are involved. It started basically with medical and veterinary interests. Hereafter the industry of functional food (fruit juice) start to use this bacteria strain quickly followed by the dairy product 'Valio Gefilus' in 1992. Valio and Oriola undertake exceptional joint venture for the Gefilus brand. Oriola-KD Corporation is a leading pharmaceutical retail and wholesale company in Northern Europe and Russia. This joint venture has resulted in non-dairy products like fruit drinks and capsules. It can be seen that when the years past products are launched to the market for new target groups like babies and kids (Food and Functionals, 2011a; Food and Functionals, 2011b).

Time line of Lactobacillus Rhamnosus (L)GG

Year	Type	Content	Effect	Industry application	Industry background of the company
1985	Patent	Human patent Lactobacillus GG	Intestine	Medicine	Gorbach and Goldin --> Pharmaceutical
1987	License	Agreement with Gorbach and Goldin	Industry		Valio --> dairy industry

Year	Type	Content	Effect	Industry application	Industry background of the company
1988	Patent	Animal based patent (Biorem C.C.)	Intestine	Medicine/Veterinary	Biorem C.C. --> Pharmaceutical & Veterinary
1989	Trademark	LGG by Valio		Dairy	Valio --> dairy industry
1990	Product Launch	Gefilus fruit juice	Intestine	Drink	Valio --> dairy industry
1992	Product Launch	Cultured buttermilk	Intestine	Dairy	Valio --> dairy industry
1993	License	first agreement between Valio and foreign players	Industry		Valio --> dairy industry
1994	License	First licensed product Vifit Campina the Netherlands	Industry	Dairy	Valio and Campina --> both dairy industry
1997	Product Launch	non-dairy products: Valio Gefilus fruit drinks and capsules	Intestine	Nutraceuticals	Valio --> dairy industry; Oriola --> Pharmaceutical
2003	Product Launch	Nutramigen, infant formula for allergic babies	Intestine	infant formula	Mead Johnsen --> infant nutrition
2004	Product Launch	product niche Valio Kidius (for kids)	Intestine	dairy	Valio --> dairy industry

Table VII: Lactobacillus Rhamnosus (L)GG

Conclusion

It can be concluded that the bacteria strain Lactobacillus Rhamnosus (L)GG can be found in many products with different industry backgrounds. It can be seen that the first interest in this strain had mainly a medical and veterinary focus. Shortly after the first couple of patents, the dairy industry became interested in this bacteria strain. Although the first application of (L)GG can be recognised in a fruit juice, many dairy companies started to use the (L)GG in their products. Technology and industry convergence can be recognised whereas dairy and the pharmaceutical industry both produce products which claim to have beneficial effect on the intestinal.

Results and Discussion

In this study a selected group of bacteria strains used in commercialized probiotic dairy products have been analysed. The different time lines of the bacteria strains, presented in the previous chapter, give an impression on how the development of the different strains lead to new products in the market.

In this chapter the research questions, presented in the beginning of this report, will be answered and discussed. Some tables will be introduced to highlight some interesting similarities and/or differences in the development process of the different bacteria strains.

To answer the question - what time it takes from patent to a final commercialized product - , it is necessary that both patent and launch data are known. In table VIII an overview is given of the different bacteria strains whereby both data have been found.

	Bifidobacterium Animalis DN-173010		**Lactobacillus Caseï DN-114001**		**Bifidobacterium lactis Bb-12**		**Lactobacillus Caseï Shirota**		**Lactobacillus Rhamnosus (LGG)**	
	Year	**Industry**	**Year**	**Industry**	**Year**	**Industry**	**Year**	**Industry**	**Year**	**Industry**
Patent or discovery	1985	Dairy	1994	Dairy	2010	Cosmetics	1930	Medical	1985	Medical
Related product launch	1987	Dairy	1996	Dairy	2008	Cosmetics	1935	Health & Nutrition	1990	Food (drink)
Time span	2		2		-2		5		5	

Table VIII: Time span from patent to commercial product

It the cases of Bifidobacterium Animalis DN-173010, Lactobacillus Caseï DN-114001, Bifidobacterium lactis Bb-12 and Lactobacillus Rhamnosus (L)GG the patent data are known. In the case of Lactobacillus Caseï Shirota only the year of discovery is known, but the development stage can be presumed as equal. The time between patent and product launch are in these cases either 2 or 5 years. In the case of Bifidobacterium lactic Bb-12 it can be seen that the product has been already launched before an official patent was claimed. As described before, the final cosmetic product does not contain the bacteria strain Bifidobacterium lactis Bb-12, but it gives relevant information for the time span. It can be analysed that when patent and product launch are managed by the same industry (or in these cases the same companies) the product launch takes fewer years than when technology has to be adopted by other industries.

In table VIII only the patents are presented which have leaded to commercialised product. In the time lines it can be seen that many other patents can be found which have not (yet) leaded to commercial products. Therefore this time span must not be used to generalize the whole development process, but should only give the impression that time between patent and

commercial products can happen relatively fast, and even faster when it happens when managed by one industry or company.

To be able to answer the questions - what industries are involved in the development of the selected bacteria strains - , and - which industry finally brings the product to the market – an overview of the different patents and product launches is needed. In table IX industries that have patented strains applications and launched probiotic products are presented. It should be mentioned that the bacteria strain Lactobacillus Caseï Shirota is not presented in this table whereas only the company Yakult works with this strain. This gives no information on how the strain develops within different industries.

Bifidobacterium Animalis DN-173010				**Lactobacillus Caseï DN-114001**				**Bifidobacterium lactis Bb-12**			
Patent		**Product**		**Patent**		**Product**		**Patent**		**Product**	
Year	**Industry**	**Year**	**Industry**	**Year**	**Industry**	**Year**	**Industry**	**Year**	**Industry**	**Year**	**Industry**
1985	Dairy	1987	Dairy	1994	Dairy	1996	Dairy	2009	Food	2007	Dairy
				2008	Dairy - Pharma			2010	Cosmetics	2008	Cosmetics
										2009	Health & Nutrition
										2011	Pharma-ceutical

Lactobacillus acidophilus LA-5				**Lactobacillus Rhamnosus (LGG)**			
Patent		**Product**		**Patent**		**Product**	
Year	**Industry**	**Year**	**Industry**	**Year**	**Industry**	**Year**	**Industry**
1977	Dairy	2007	Dairy	1985	Medical	1990	Dairy
1978	Pharma - Veterinary	2007	Pharma-ceutical	1988	Veterinary	1992	Dairy
1983	Veterinary					1997	Pharma-ceutical
1989	Medical					2003	Infant Nutrition
1991	Medical					2004	Dairy

Table IX: Patents and products

When analysing the industries that are involved in the development process based on patent information, it can be concluded that the following industries show the main interest in the analysed bacteria strains:

- Medical/Pharmaceutical industry
- Food/Dairy industry
- Veterinary industry
- Cosmetic industry

When analysing the development process of probiotics as a whole it can be seen that in the 70's and 80' most patents had medical and veterinary background. It can be presumed that technology adoption by the dairy and food industry took some years. Also it can be analysed that the veterinary industry has mainly be active in the early development stage of some probiotic strains. Nowadays, probiotics are widely described in terms of animal applications, but these applications have different goals and involve different bacteria strains. Ortwin (2005) has described the difference of probiotic use between human an animal applications. In table X an overview of these differences is given. More recently the cosmetic industry started to show interest in the probiotic field. L'Oreal has patented some applications with even new claims. Where most probiotic patents claim to have effect on the intestine, L'Oreal claims to have found strains which benefit the skin condition.

	Human nutrition	**Animal nutrition**
Goal	Long term effects	Quick response
Effectiveness	Difficult to assess	Easy to assess
Characteristics of intake	In combination with a small portion of food	As additive in mixed feed
Frequency of intake	Once per day or more?	10 to 20 times per day
Microorganisms (most frequent)	*Lactobacillus spp.*	*Enterococcus faecium*
	Bifidobacterium spp.	*Bacillus spp.*
	Enterococcus spp.	*Saccharomyces cerevisiae*
Natural habitat	Digestive tract, milk products	Digestive tract, soil, fruits

Table X: Probiotics in animal versus human applications (Ortwin, 2005)

When analysing the industries that finally bring products to the market, it can be concluded that the dairy and pharmaceutical industry are the main player. Recently the cosmetic industry started to launch some products, but still is a small player in the probiotic market.

To be able to answer the questions - can technology and industry convergence be recognised in the development process -, the probiotic market should be analysed as a whole. When looking at table VIII it can be concluded that the discovery and development of the analysed probiotic strains, mainly show medial background. This shows that technology convergence has taken place whereby the dairy industry has adopted medical knowledge which has resulted in new patents. Whereas the medical industry show limited intentions to launch products based on their finding, the dairy industry used this knowledge to develop new products. This technology convergence together with new demand for healthy foods has resulted in the launch of probiotic dairy products. Whereas the analysed bacteria strains in the beginning mainly have been used in dairy products, the dairy industry can be seen as innovators using probiotic strains for new products. The dairy industry has stand on the beginning of more technology convergence and even industry convergence. In table XI patents, products launches and additional data give information how other industries start to show interest in the use of probiotics, whereby technology and industry convergence become visible. A clear example of industry convergence is the case of Bifidobacterium Lactis Bb-12. Here it can be seen that both the dairy industry and the pharmaceutical industry launched products to the probiotic market which claims to have similar effects. It can be presumed that especially consumers will consider these kinds of probiotic products as relatively equal and interchangeable. This can also be explained as converge in substitutes which make concrete boundaries between products and industries very vague. In the case of Bifidobacterium Lactis Bb-12 even the cosmetic industry show interest in the strain and have patented applications containing this strain. This shows that different industries start to be active in the probiotic market using the same technology. In contrast, the case of Lactobacillus Caseï Shirota shows how one company, Yakult, starts to launch products into markets of different industries. The total amount of products that are launched to the market containing a specific strain really depend on how the companies with different backgrounds show willingness to collaborate with each other. In the case of Bifidobacterium lactis Bb-12 and Lactobacillus acidophilus LA-5, which are strains manufactured and sold by Christian Hansen, it can be concluded that much more product launches can be found containing these strains. This can be related to the co-operation between Christian Hansen and companies that would like to launch probiotic products. Christian Hansen shares their knowledge with other companies, basically to increase their sales amounts of the bacteria strains. These kinds of activities can be described as synergy whereby individual talents and efforts are combined to create new products from which both companies can benefit. In the case of LGG it can be seen that many different products have been launched (see appendix II). This can be due to the fact that Valio sell licences whereby other companies can benefit from the strong trademark LGG.

Lactobacillus Caseï DN-114001

Technology convergence:

Year	Content	Type	Industry
2005	Joint research		Dairy - medical
2008	Patent	Treatment	Dairy - medical

Bifidobacterium lactis Bb-12

Technology convergence:

Year	Content	Type	Industry
2009	Patent	Infant formula	Food company
2010	Patent	Food supplement	Cosmetic

Industry convergence

Year	Content	Type	Industry
2009	Product launch	Food supplement	Health & Nutrition
2011	Product launch	Food supplement	Pharmaceutical

Lactobacillus acidophilus LA-5

Technology convergence:

Year	Content	Type	Industry
1983	Patent	Feed mixture	Veterinary
1989	Patent	Method of selection	Medical
1991	Patent	Strain	Medical

Industry convergence

Year	Content	Type	Industry
2007	Product launch	Food supplement	Pharmaceutical

Lactobacillus Caseï Shirota

Technology convergence:

Year	Content	Type	Industry
1963	Research	Cosmetics	Health & Nutrition

Industry convergence

Year	Content	Type	Industry
1971	Product launch	Cosmetics	Health & Nutrition
1975	Product launch	Pharmaceutical	Health & Nutrition
1979	Product launch	Pharmaceutical	Health & Nutrition

Lactobacillus Rhamnosus (LGG)

Technology convergence:

Year	Content	Type	Industry
1985	Patent		Medical
1988	Patent		Medical - Veterinary

Industry convergence

Year	Content	Type	Industry
1997	product launch	Drinks & capsules	Dairy - Pharma
2003	product launch for allergic babies		Infant nutrition

Table XI: Signs of technology and industry convergence

From a management point of view it can be concluded that technology development in the probiotic market is a slow process. Whereas the benefits of good bacteria for intestinal health has already discovered by Metchnikoff round 1908, the first probiotic product was launched by Yakult in 1935. From here the interest in probiotics has intensively grow. Nevertheless it took quite some time before the second product (based on researched bacteria strains) was launched on the market. In 1990 Valio introduced a probiotic juices followed-up with a butter-milk in 1992. From here, many companies have entered the probiotic market. The different industries are patenting lots of different bacteria strains with multiple applications. Especially Christian Hansen and Yakult are good examples of companies that have patented many bacteria strains. In the lime lines of the analysed bacteria strains only the first patents, which show some relation with probiotic applications, have been included. When searching for other patents on the bacteria strains, many can be found. Basically, most patents involve technical issues around the manufacturing of bacteria strains. They describe how certain bacteria should be selected and prepare them for new applications. The amount of bacteria strains which are finally used in probiotic products are very limited compared too many different bacteria species subspecies and strains described in the mass of available patents. This makes it difficult to analyse the total process of PD and R&D in the probiotic sector. Whereas in this study only a very limited amount of patents and products have been analysed, the presented data should be considered as a small piece of the total probiotic development process. Another aspect which makes it difficult to analyse the bacteria strains, is that patents often are very general descriptions in relation to the bacteria strains used. They often give many examples of bacteria strains which might be used to fulfil the aim of the patented application. Hereby it can be concluded that not the bacteria strains are the most important content of a patent, but the manufacturing process around them. This makes research into a particular bacteria strain difficult. Often scientific databases and patent databases uses searching methods whereby words in the abstract and key words are most important. Often the involved bacteria strains are not even mentioned in the abstracts or key words. Thereby the reference towards a certain bacteria strain can be done in several ways. Often the patent will describe something like 'bacteria from the species lactobacillus will be used'. This does not say anything about the particular strain which is used in the application. Another problem occurs when the strains are described differently in the patent than expected. Often not the full name of the bacteria strain is used, but the ATCC coding (American Type Culture Collection). Thereby the problem can be found that bacteria strain will change codes when in research is found that two different bacteria strains are actually very similar strains (this has been described in the case of Bifidobacterium lactic Bb-12). All those aspects together make the research process into probiotic bacteria strains very difficult.

Future research

This study can be seen as a start for further research in this field. It would be interesting to research more different bacteria strains to see how the different industries and technologies are influencing each other. In this study only some bacteria strain used in commercial dairy products have been analysed, but during the process many other probiotic applications and products have been found. Those are not described in this report because they use other strains. Nevertheless, it would be interesting to research these products to analyse what time and technology convergence affect the development process. Whereas the research into products and patents can be described as time consuming and complex it may even take a few years to conduct a research which will present structured and real scientific results.

When analysing the food & agriculture industry and in particular the dairy industry it can be concluded that many commercial products containing probiotics can be seen as substitutes. When one product will increase in price it is possible that consumers will chose a similar probiotic dairy product or even will chose for a food supplement which claims the same health effect. From a complementary point of view it can assumed that pharmaceutical products like antibiotic or other medication, could have a relation on the demand of probiotics. NCCAM (national center for complementary and alternative medicine, 2011) refer to the fact that probiotics can be used as complementary and alternative medicine. Not only the similarity of the products in the market is an interesting case, also the consumer differences would be interesting to research for strategic managers in the industry. It can be concluded that cultural differences around the world lead to a different consumer adaptation towards probiotic products. Franke (2011) argues that is has been possible for Yakult to be adopted quickly in the Japanese market due to life style. In the Japanese culture it is more accepted to use products which may result in health benefits on the long-term, whereas in western countries people most often search for short term solutions when a certain health problem rises.

Al those aspects together make the probiotic market a complex but interesting research case which may lead to new knowledge on how industry convergence develops and can be recognised. This could help future managers to recognise changes in the industry more quickly and hopefully give them the opportunity to respond to the market adequately.

References

Actimel (2011) Het verschil tussen Activia van Danone en Actimel van Danone. [www document] http://www.actimel.nl/vraagenantwoord.html accessed on 11 July 2011.

Activia (2011) *Who discovered BL Regularis* [www document] http://www.activia.ca/en/FAQ/ accessed on 16 may 2011).

Belbe G. M. (2009) Groupe Danone [pdf document] http://www.scribd.com/doc/44290501/Dan-One accessed on 18 april 2011.

Boehlje M., Bröring S. (2011) *Patentanalyse zur aufdeckung von trends (technologiekonvergenz)* [www document] http://www.al.hs-osnabrueck.de/32455.html?&L=1 accessed on 7 july 2011.

Brid K. (2008) Probiotic supplements may help sensitive skin [www document] http://www.cosmeticsdesign-europe.com/Formulation-Science/Probiotic-supplements-may-help-sensitive-skin 13 July 2011.

Bröring S. (2010) *Developing innovation strategies for convergence - is 'open innovation' imperative?* Int. J. Technology Management, Vol. 49, Nos. 1/2/3, 2010.

Bröring S., Leker J. (2007) *Industry Convergence and Its Implications for the Front End of Innovation: A Problem of Absorptive Capacity*. Creativity and innovation management Vol. 16 No. 2 2007 pp. 165-175.

Bröring S., Cloutier M., Leker J. (2006) *The front end of innovation in an era of industry convergence: evidence from nutraceuticals and functional foods*. R&D Management Vol. 36, No. 5, 2006, pp. 487-498.

Bezzina J., Sanches B. (2005) Technological convergence and regulations - challenges facing developing countries. [pdf document] http://www.google.nl/url?sa=t&source=web&cd=12&ved=0CGUQFjAL&url=http%3A%2F%2Fwww.infodev.org%2Fen%2FDocument.1.pdf&rct=j&q=technology%20convergence&ei=rvTlTe6VFsPssgaQ4MSkCA&usg=AFQjCNGiO1NynwUsWU2MH02JwypBUVLcfQ accessed on 26 may 2011.

Building Danone (1996) Building Danone – 30 years of passion. [pdf document] http://www.danone.com/en/company/history.html chapter 5 accessed on 9 august 2011.

CDRF (2007) *Commercial Strains Sold As Probiotics* [www document] http://www.usprobiotics.org /products.asp accessed on 6 may 2011.

Chain Innovation (2010) *Patentanalyse zur aufdeckung von trends (technolgiekonvergenz)* [www document] retrieved from: http://www.chainnovation.de/ - Patentanalyse. accessed on 22 March 2011.

Choi, D., Valikangas, L. (2001) *Patterns of Strategy Innovation*. European Management Journal Vol. 19, No. 4, pp. 424-429.

Curran C-S., Leker J. (2011) Patent indicators for monitoring convergence - examples from NFF and ICT. Technological Forecasting & Social Change 78 (2011) pp. 256-273.

Curran C-S., Bröring S., Leker J., (2010) *Anticipating converging industries using publicly available data.* Technological Forecasting & Social Change 77 (2010) pp. 385-395.

Danilovic M., Browning T. R., (2007) *Managing complex product development projects with design structure matrices and domain mapping matrices.* International Journal of Project Management 25 (2007) pp. 300-314.

Danone (2011) *Brand stories* [www document] http://www.danone.com/en/brands/brand-stories.html accessed on 18 april 2011.

Danone Geschiedenis (2010) *Geschiedenis van Groupe Danone* [www document] http://www.danone.nl/Bedrijf/Geschiedenis.aspx accessed on 11 July 2011.

Danone Reserach (2008) *Translate your scientific knowledge to create a world of healthier food* [pdf document] http://www.danone.com/images/pdf/plaquette%20v4%20gb%20f.pdf accessed on 18 april 2011.

Danisco (2011a) *Danisco in Brief* [www document] http://www.danisco.com/about_us/danisco_in_brief/ accessed on 14 July 2011.

Danisco (2011b) *More on Probiotics* [www document] http://health.danisco.com/health_and_nutrition/product_range/howarur_premium_probiotics/more_on_probiotics/ 14 July 2011.

DermaHarmony (2011) *Probiotics* [www document] http://www.dermaharmony.com/skinnutrition/probiotics.aspx accessed on 14 July 2011.

Eufic (2006) *Functional foods – the basics*- Retrieved from: http://www.eufic.org/article/en/expid/basics-functional-foods/ accesses on 16 March 2011.

Euromonitor International (2011*) Yoghurt in the US* [www document] http://www.euromonitor.com/yoghurt-in-the-us/report accessed on 4 May 2011.

FAO/WHO (2002) *Guideline for the Evalutaion of Probiotics in Food* [pdf document] ftp://ftp.fao.org/docrep/fao/009/a0512e/a0512e00.pdf accessed on 1 July 2011.

Food-Info (2011) *Probiotics* Retrieved from http://www.food-info.net/uk/ff/probiotics.htm accessed on 28 March 2011.

Food and Functionals (2011a) *Gefilus® supplements in a safe pair of hands* [www document] http://asiakaslehti.com/foodsandfunctionals/node/44 accessed on 25 May 2011.

Food and Functionals (2011b) *Valio Gefilus 20 years* [www document] http://asiakaslehti.com/foodsandfunctionals/node/43 accessed on 11 August 2011.

Franke, L. (2011) *Personal contact with Lidwien Franke who is Assistant Science Manager of Yakult NL.* Information obtained during excursion at Yakult in Almere 18 may 2011.

Gambardella A., Torrisi S. (1998) *Does technological convergence imply convergence in markets? Evidence from the electronics industry*. Research Policy 27 (1998) pp. 445-463.

Hansen CHR (2011a) *Probiotics for dietary supplements* [www document] http://www.chr-hansen.com/campaign_sites/probiotics_for_human_health/our_probiotic_products/strains/bb_12r.html accessed on 21 april 2011.

Hansen CHR (2011b) *Yovis Regola* [www document] http://www.chr-hansen.com/products/product_areas/probiotics_for_human_health/customer_case_stories/sigma_tau_italy.html accessed on 10 August 2011.

Hansen CHR (2011c) *LA-5* [www document] http://www.chr-hansen.com/products/product_areas/probiotics_for_human_health/strains/la_5r.html accessed on 10 August 2011.

Hansen CHR (2011d) *LIVEO* [www document] http://www.chr-hansen.com/products/product_areas/probiotics_for_human_health/customer_case_stories/sagitus_latvia.html accessed on 11 august 2011.

Hansen P.A., Mocquot G. (1970) *Lactobacillus Acidophilus.* International Journal of Systematic Bacteriology Vol. 20 No. 3 pp. 325-327.

Hayes D. (2011) *Yakult's gut instinct for success: the continued recession in Japan has not impeded probiotic giant Yakult Honsha.* [www document] http://goliath.ecnext.com/coms2/gi_0199-14871984/Yakult-s-gut-instinct-for.html accessed on 11 august 2011.

Inneov (2011) *De Laboratoires innéov* [www document] http://www.inneov.be/nl/index.html accessed on 13 July 2011.

Institut Pasteur (2011) *Mission of the Institut Pasteur* [www document] http://www.pasteur.fr/ip/easysite/pasteur/en/institut-pasteur/mission accessed on 12 July 2011.

Kaluza, B., Blecker Th., Bischof Ch. (1998) *Strategic Management in Converging Industries.* Discussion paper of the college of Business Administration University of Klagenfurt, Austria.

Katz, L.M. (1996) *Remarks on the Economic Implications of Convergence.* Industrial and Corparate Change Vol. 5 No. 4 1996 pp 1079-1095.

Kotler P., Keller, K.L. (2006) *Marketing Management 12e edition.* Pearson Eduction, Inc. Upper Saddle River, New Jersey.

Krutmann J. (2009) *Pre- and probiotics for human skin.* Journal of Dermatological Science 54 (2009) pp. 1-5.

Lei, D.T. (2000) *Industry evolution and competence development: the imperatives of technological convergence.* Int. J. Technology Management, Vol. 19, Nos. 7/8, 2000

Lind J. (2005) *Ubiquitous Convergence: market redefinitions generated by technological change and the Industry Life Cycle.* Paper for the DRUID Academy Winter 2005 Conference, January 27-29, 2005.

L'Oreal (2004) *Active Cosmetics* [pdf document] http://www.loreal-finance.com/site/us/contenu/rapport/rapport2004/Active_Cosmetics.pdf accessed on 9 august 2011.

Mark-Herbert C. (2004*) Innovation of a new product category - functional foods* -. Technovation 24 (2004) pp. 713-719.

Marketsandmarkets (2010) Global Probiotics Market. Retrieved from Prof. Dr. S. Bröring.

Masco, L., Ventura, M., Zink, R., Huys, G., Swings, J. (2004) *Polyphasic taxonomic analysis of Bifidobacterium animalis and Bifidobacterium lactis reveals relatedness at the subspecies level: reclassification of Bifidobacterium animalis as Bifidobacterium animalis subsp. animalis subsp. nov. and Bifidobacterium lactis as Bifidobacterium animalis subsp. lactis subsp. nov.* International Journal of Systematic and Evolutionary Microbiology Vol. 54 no. 4 (2004), pp. 1137-1143.

Meer van der T. (2008) *Unilever UK lanceert probiotica-ijsjes.* [www document] http://www.evmi.nl/nieuws/marketing-sales/5258/unilever-uk-lanceert-probiotica-ijsje-.html 9 July 2011.

NCCAM (2011) *Probiotics* [www docement] http://nccam.nih.gov/health/probiotics/ accessed on 31 may 2011.

Nebraska Cultures (2011) *Khem Shahani* [www document] http://www.nebraskacultures.com/htmls/dr_shahani.html accessed on 14 July 2011.

Nestlé (2006) *Food and Nutrition - Communication* - [pdf document] http://www.research.nestle.com.cn/scienceinaction/HealthySkin.pdf accessed on 14 august 2011.

Nobel Media AB (2011) *Biography Ilya Mechnikow* [www document] http://nobelprize.org/nobel_prizes/medicine/laureates/1908/mechnikov-bio.html assecced on 29 June 2011.

Ortwin S. (2005) *Micro-Organisms as Feed Additives - Probiotics.* Advances in Pork Production Volume 16, (2005) pg. 161.

Oxford Dictionaries Online (2011) *converge* [www document] http://english.oxforddictionaries.com/definition/converge accessed on 7 July 2011.

Patentstorm (2011) *Fermented milk product containing viable bifidocateria.* [www document] http://www.patentstorm.us/patents/4091117/description.html accessed on 3 May 2011.

Saarela M., Mogensen G., Fondén R., Mättö J., Mattila-Sandholm T. (2000) *Probiotic bacteria: safety, functional and technological properties.* Journal of Biotechnology 84 (2000) pp. 197–215.

Sanders M. E. (2007) *Probiotics* Diary & food Culture Technologies Nov. 2007.

Siezen R.J., Wilson G. (2010) *Probiotics genomics.* Microbial Biotechnology, 3 (1), pp. 1-9.

Simon O. (2005) *Micro-Organisms as Feed Additives - Probiotics.* Advances in Pork Production (2005) Vol. 16, pp 161-167.

Schermerhorn, J.R. (2008) *Management 9e.* John Wiley & Sons, Inc. Hoboken.

Szajewska H. (2010) *Probiotics and Prebiotics in Preterm Infants: Where are we? Where are we going?* Early Human Development 03210 2010.

Terry C., (year unknown) *The Interrelationships Between Markets* [pdf document] http://www.chris-terry.com/Micro/010%20THE%20INTERELATIONSHIPS%20BETWEEN%20MARKETS.pdf accessed on 30 may 2011.

TradeMarkia (2011) *TransAgra International Inc.* [www document] http://www.trademarkia.com/company-transagra-international-inc-1254651-page-1-2 accessed on 13 July 2011.

United States District Court (2009) *Demand for Jury Trail - General Mills, Inc., and Yoplait USA, INC.* [pdf document] http://www.classactionlitigation.com/YoplusComplaint.pdf accessed on 2 May 2011.

USANA (2009) *Usana launches new probiotic food supplement* [www document] http://mlmblog.net/site/2009/10/usana-launches-new-probiotic-food-supplement-html accessed on 13 July 2011.

Valio Ltd (2011a) *The history of Lactobacillus GG and Valio Gefilus* [www document] http://ammattilaiset.valio.fi/portal/page/portal/valiocom/valio_worldwide/innovations/lactobacillus_gg13042011151809/history13042011152352 accessed on 25 may 2011.

Valio Ltd (2011b) *Where did Gefilus products come from?* [www document] http://ammattilaiset.valio.fi/portal/page/portal/valiocom/company_information/products_international_sales/functional_products18102006164724/lactobacillus_gg19102006134654/valio_gefilus_20_years03032010171139?i_sessio=A1F428242CD473C55C9C29572097F1E1 accessed on 11 august 2011.

Valio Ltd (2011c) *Products with LGG* [www document] http://ammattilaiset.valio.fi/portal/page/portal/valiocom/valio_worldwide/innovations/lactobacillus_gg

13042011151809/lgg%C2%AE_material15042011123710/lgg%20brands_25022011_0.pdf assessed on 25 may 2011

Vasiljevic T., Shah N.P. (2008) *Probiotics—From Metchnikoff to bioactives.* Int. Dairy Journal 18 (2008) pp. 714– 728.

Walsh, V., Lodorfos G. (2002) *Technological and Organizational Innovation in Chemicals and Related Products.* Journal of Technology Analysis & Strategic Management, Vol. 14, No.3, 2002.

Weaver B., (2007) *Industry Convergence - Driving forces, factors and consequences* -. Paper submitted tot the 19th NFF conference in Bergen, 9-11 August 2007.

Weirich A., Hoffmann G.F. (year unkown) *Ernst Moro (1874 - 1951).* European Journal of Pediatrics Vol. 164 No. 10 pp 599-606.

World Gastroenterology Organisation (2008) *Probiotics and probiotics* [pdf document] http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/19_probiotics_prebiotics.pdf accessed on 21 april 2011.

Yakult (2011a) *Joint Venture* [www document] http://www.yakult.co.in/index.php?option=com_frontpage&Itemid=1 accessed on 26 may 2011.

Yakult (2011b) *History* [www document] http://www.yakult.co.jp/english/company/history.html accessed on 11 August 2011.

Yakult (2011c) *dr. Minoru Shirota* [www document] http://www.yakult.nl/#/kennis-en-wetenschap/dr-minoru-shirota/ accessed on 4 May 2011.

Yakult (2011d) *Yakult Company Profile* [pdf document] http://www.yakult.co.jp/english/pdf/profile2010-2011.pdf accessed on 19 may 2011.

Yakult (2011e) *Yakult Danone plans to bring probiotic foods* [www document] http://www.yakult.co.in/index.php?option=com_content&task=view&id=82&Itemid=81 accessed on 12 August 2011.

Yamaguishi C.T., Michele S.R., De Dea Lindner J., Soccol V.T., Soccol C.R. (2011) *Current Market Trends and Future Directions.* Microbiology Monographs (2011), Vol. 21, pp 299-319.

Yoplait (2007a) *A fact Sheet for Health Professionals* [pdf document] http://www.yoplus.com/pdf/HPS.pdf accessed on 20 april 2011.

Yoplait (2007b) *Yoptial Immuni+ enters the ract* [www document] http://www.yoplait.ca/en/quoi_neuf_all.aspx?Id=101 accessed on 3 May 2011.

Ziemer C.J., Gibson G.R. (1998). *An Overview of Probiotics, Prebiotics and Synbiotics in the Functional Food Concept: Perspectives and Future Strategies.* International Dairy Journal 8 (1998) pp. 473-479.

Patents

Andersen et al. 4020185 issued on 26 April 1977 [www document] http://www.patentstorm.us/patents/4020185/desciption.html

Biorem C.C ZA1987/09287 published on 27 July 1988 [www document] http://www.wipo.int/patentscope/search/en/detail.jsf?docId=ZA4517322&recNum=1&maxRec=1452&office=&prevFilter=&sortOption=App+Date+Asc&queryString=dairy+product+probiotic&tab=NationalBiblio

WO 96/020607 deposited on 30 december 1994 [pdf document]
http://www.sumobrain.com/patents/wipo/Milk-starter-culture-use-thereof/WO1996020607A1.pdf

EP 1838158 B1 published on 16 Ju;y 2008 [www document] http://ip.com/patent/EP1838158B1

Farmos-Yhtyma 4689226 published on 5 July 1983 [pdf document] retrieved from:
http://www.google.com/patents?id=HKU8AAAAEBAJ&printsec=frontcover&dq=4689226&hl=en&ei=U9hCToTHNcHsOem-ubIJ&sa=X&oi=book_result&ct=result&resnum=1&ved=0CCkQ6AEwAA

Gorbach and Goldin 4839281 issued on 13 June 1989 [www document]
http://www.patentstorm.us/patents/4839281/claims.html

Gorbach and Goldin 4839281 published on 13 June 1989 retrieved from:
http://www.google.com/patents?id=KSAsAAAAEBAJ&printsec=frontcover&dq=4839281&hl=en&ei=V9lCTp6uEM3tOZWI3akJ&sa=X&oi=book_result&ct=result&resnum=1&ved=0CCkQ6AEwAA

Gorbach and Golding 5032399 published on 16 July 1991 retrieved from:
http://www.google.com/patents?id=xuwgAAAAEBAJ&printsec=frontcover&dq=5032399&hl=en&ei=ttlCTuC8LY30-gb84om5CQ&sa=X&oi=book_result&ct=result&resnum=1&ved=0CCkQ6AEwAA

L'Oreal 7651680 (2010) published on 26 January 2010 [pdf document]
http://www.google.com/patents?id=cbHLAAAAEBAJ&pg=PA2&dq=skin-probiotic&hl=en&ei=VMpHTof_PMia-wbv9vH5Bg&sa=X&oi=book_result&ct=result&resnum=1&ved=0CCkQ6AEwAA#v=onepage&q&f=false

Nestec 20090304655 published on 12 October 2009 [www document]
http://www.faqs.org/patents/app/20090304655

TransAgra 4349569 published on 14 September 1982 [www document]
http://www.patentstorm.us/patents/4349569/claims.html

Yakult BRPI6684297 published on 10 July 1973 [www document]
http://www.wipo.int/patentscope/search/en/detail.jsf?docId=BR5887247

Trademarks

Bb-12 (1999) Bifidobacterium Bifidum (Lactis) strain for use as a dietary supplement in the human health industry [www document] http://healthcare.zibb.com/trademark/bb-12/29740161

Bifidus BL (2007) Dietetic foodstuffs and beverages adapted for medical use; food for babies; nutritional supplements for medical and dietary purposes [pdf document] the document can be retrieved from:
http://tdr.uspto.gov/search.action?sn=78482852

LA-5 (1997) bacteriological preparations containing lactobacillus acidophilus in the dairy industry [www document] http://www.trademarkia.com/la5-75229365.html

Appendix I: Product overview Yakult

Products containing *L. casei* strain Shirota (Fermented milk drinks)

Yakult 400
Contains 40 billion *L. casei* strain Shirota per bottle.
Potent protection for intestinal health.

Yakult 400LT
Yakult 400 with reduced sweetness and fewer calories.
Contains 40 billion *L. casei* strain Shirota per bottle.

Yakult
A Probiotics pioneer. For people of all ages, including children and the elderly.

Yakult Calorie Half
For customers who prefer fewer calories and less sweetness. All the benefits of Yakult with a great new taste and half the calories and sweetness of our original product.

Yakult 300V
Contains 30 billion *L. casei* strain Shirota per bottle.
Also includes vitamins C and E.

Pretio
Contains at least 10 mg of GABA per pack. A fermented milk drink recommended for people with high blood pressure.

Yakult SHEs
Offers iron and calcium, in addition to collagen. Recommended for women in particular.

Products containing *L. casei* strain Shirota (Fermented milk products)

Yakult SHEs Hard Type
Contains collagen, iron, and calcium.
A new texture created from gelatin and agar.

Products containing *L. casei* strain Shirota (Fermented milk)

Joie
Yogurt drink containing live *L. casei* strain Shirota and calcium. Plain and fruit-flavored varieties.

Sofuhl
Dessert yogurt containing *L. casei* strain Shirota.

Purela
Soft yogurt containing *L. casei* strain Shirota and Aloe Vera pulp.

Source: Yakult Company Profile 2010-201

Appendix III Products with LGG

Country	Company	Brand	Product types	Launching year	Type
Finland	Valio Ltd	Valio Gefilus	Fermented whey drink, Fermented milk, Milk, Juice drink, Fruit-based daily dose drink	1990	diary
		Valio Kidius Gefilus	Yoghurt, Drinking yoghurt	2004	diary
		Valio Viilis Gefilus	Viili fermented milk with fruit	2010	diary
The Netherlands	FrieslandCampina	Campina Vifit	Yoghurt, Drinking yoghurt	1994	diary
Norway	Tine BA	Biola	Fermented milk Drinking yoghurt	1995	diary
		Biola Pluss	Yoghurt	2010	diary
Switzerland	Emmi AG	Aktifit	Fermented milk (mini bottle)	1996	diary
			Yoghurt	2010	diary
Ecuador	Industrias Lacteas Toni S.A.	Toni	Yoghurt, Drinking yoghurt	1996	diary
		Toni Vivaly	Drinking yoghurt	2008	diary
Japan	Takanashi Milk Products Co., Ltd.	Onaka He GG!	Fermented milk drink, Yoghurt	1996	diary
		LGG	Fermented milk drink, Yoghurt		diary
Australia	Parmalat Australia Ltd	Vaalia	Yoghurt, Drinking yoghurt	1997	diary
		Vaalia Innergy	Drinking yoghurt (mini bottle)	2010	diary
Italy	Granarolo S.p.A.	YOMO Rinforzo	Fermented milk (mini bottle)	1998	diary
Iceland	Mjólkursamsalan	LGG+	Fermented milk (mini bottle)	1998	diary
			Yoghurt	2007	diary
Croatia, Bosnia-Herzegovina, Slovenia	DUKAT	b'Aktiv	Yoghurt, Drinking yoghurt	1998	diary
Israel	Tnuva Dairy Products	White Yoplait	Yoghurt	1998	diary

		Yoplait 360o	Yoghurt drink for children	2007 diary
Korea	Maeil Dairy Industry Co., Ltd.	Maeil Active GG	Drinking yoghurt	1998 diary
		Maeil PURE	Drinking yoghurt	2010 diary
Estonia	Valio	Valio Gefilus	Fermented milk (Kefir), Yoghurt, Juice Drink	1999 diary
Greenland	Mjólkursamsalan	LGG+	Fermented milk (mini bottle)	1999 diary
Papua-New-Guinea	Parmalat Australia Ltd	Vaalia	Yoghurt	2000 diary
Russia	Valio	Valio Gefilus	Yoghurt, Fermented milk, Juice Drink	2000 diary
		Valio Kidius Gefilus	Yoghurt	2000 diary
	Unimilk	BioBalans	Drinking yoghurt, Fermented milks , (Kefir, Tan), Fruit quark, fruit yoghurt	2009 diary
	Unimilk	Tema	Children's yoghurt, Quark	2010 diary
Spain	Kaiku / Iparlat	Kaiku Actif	Fermented milk drink	2001 diary
Ireland	Glanbia Plc.	Yoplait everybody	Drinking yoghurt	2001 diary
		Yoplait everykid	Drinking yoghurt	2005 diary
Northern Ireland	Glanbia Plc.	Yoplait everybody	Drinking yoghurt	2001 diary
United Arab Emirates	Al Ain Dairy	Al Ain Gefilac Laban	Fermented milk	2001 diary
Uruguay	Conaprole	Vital+	Drinking Yoghurt	2002 diary
Latvia	Valio	Valio Gefilus	Fermented milks	2003 diary
Serbia, Montenegro	DUKAT	b'Aktiv	Yoghurt, Drinking Yoghurt	2003 diary
Lithuania	Valio Ltd	Valio Gefilus	Yoghurt, Fermented Milk (Kefir)	2003 diary
Chile	Surlat	Bio Kaiku	Yoghurt	2004 diary
Macedonia	DUKAT	b'Aktiv	Yoghurt	2004 diary
Vietnam	Campina Vietnam	Campina YoGood	Yoghurt	2004 diary
Vanuatu	Parmalat Australia	Vaalia	Yoghurts	2008 diary

Kosovo	DUKAT	b'Aktiv	Yoghurt, Drinking Yoghurt	2008	diary
Ukraine	Unimilk	BioBalans	Fermented milks	2009	diary
Kazakhstan	Unimilk	BioBalans	Kefir, Drinking yoghurt	2009	diary
			Yoghurts	2010	diary
Albania	Dukat	B'Aktiv	Yoghurt, Drinking yoghurt	2009	diary
USA	Danone		Yoghurts	2009	diary
Argentina	Mastellone	La Serenisima	Cheeses with LGG®	2010	diary
Finland	Oriola	Gefilus Plus, Gefilus Basic	Hard gelatine capsules	1997	supplements
		Gefilus drops	Drops in oil	2009	supplements
U.S.A.	Amerifit Brands	Culturelle	Hard gelatine capsules	1998	supplements
Estonia	Oriola	Gefilus Plus, Gefilus Basic	Hard gelatine capsules	1998	supplements
Germany	InfectoPharm GmbH	InfectoDiarrstop LGG®	ORS + Lactobacillus GG in powder (registered drug)	2000	supplements
		InfectoDiarrstop LGG ®Mono	Lactobacillus GG in powder (registered drug)	2006	supplements
		LGG® capsules	Hard gelatine capsules	2001	supplements
Lithuania	Oriola	Gefilus Plus, Gefilus Basic	Hard gelatine capsules	2000	supplements
Malaysia	Paedicare Sdn Bhd	Lacto GG	Hard gelatine capsules	2003	supplements
Latvia	Oriola	Gefilus Basic	Hard gelatine capsules	2004	supplements
Norway	Ferrosan	Idoform Immuno	Chewing tablet with vitamins	2005	supplements
		Idoform Balance	Chewing tablet with vitamins	2008	supplements
Russia	Ferrosan	Bifiform Kids	Chewing tablet with vitamins	2005	supplements
		Bifiform Kids	Powder with vitamins	2005	supplements
		Bifiform Complex	tablets	2008	supplements
		Multi-tabs Immuno	Multivitamine tablets	2005	supplements

		Multi-tabs Immuno Kids	Multivitamine tablets	2005	supplements
Singapore	Paedicare Sdn Bhd	Lacto GG	Hard gelatine capsules	2005	supplements
Hungary	Ferrosan	Multi-tabs Immuno	Multivitamine tablets	2005	supplements
		Multi-tabs Immuno Kids	Multivitamine tablets	2005	supplements
Czech	Ferrosan, S&D Pharma	Bifiform Kids	Multivitamine tablets	2006	supplements
		Multitabs	Multivitamine tablets	2006	supplements
		Probio-FIX Immuno	Capsules	2009	supplements
Poland	Ferrosan, Farma-Projekt	Multitabs Immuno Kids	Multivitamine tablets	2006	supplements
		Idoform Kids	Multivitamine tablets	2006	supplements
		Lactiv Baby	Drops in oil	2010	supplements
Ukraine	Ferrosan	Bififorms Kids	Multivitamine tablets	2006	supplements
		Bifiform Kids	Powder with vitamins	2007	supplements
		Bifiform Complex	Tablets	2008	supplements
Australia	Health World	Metagenics Ultra Flora Inner Health	Probiotic powder and capsules	2008	supplements
	Blackmores	Daycare Defence	Powder	2009	supplements
New Zealand	Health World	Metagenics Ultra Flora Inner Health	Probiotic powder and capsules	2008	supplements
	Natural Health Laboratories	MultiFlora	Capsules	2009	supplements
Sweden	Ferrosan	Bifiform Balance	Multivitamine tablets	2009	supplements
Denmark	Ferrosan	Bifiform Balance	Multivitamine tablets	2007	supplements
		Multikids			supplements
Romania	Ferrosan	Bifiform Kids	Multivitamine tablets	2009	supplements
Turkey	Ferrosan	Bifiform sachets	Powder with vitamins	2009	supplements

Slovakia	S&D Pharma	Probio-FIX Immuno	Capsules	2009	supplements
Hong Kong	Paedicare Sdn Bhd	Lacto GG	Hard gelatine capsules	2009	supplements
	Pro-Health		Capsules	2009	supplements
Italy, USA, UK, France, Germany, UK, France, Germany, The Netherlands	Solgar	Advanced 40+ Acidophilus Vegetable Capsules, Multi-Acidophilus Powder, Advanced Multi-Billion Dophilus Vegetable Capsules	Capsules Powder Capsules	2010	supplements
Taiwan	Muco-Relax	Trifactor	Capsules	2010	supplements
Croatia, Slovenia, Bosnia and Herzegovina , Macedonia, Serbia, Montenegro	Jadran Galenski	Normia	Powder in sticks	2010	supplements
The Netherlands, Sweden, Denmark, Germay, Italy, Belgium, Spain, Finland, Poland, France, Porugal	Mead Johnson Nutrition	Nutramigen 1 & 2 LGG® Lipil	Infant formula for allergic babies (hydrolysed formula)	2003	powder
USA	Mead Johnson Nutrition	Nutramigen2 Lipil with Enflora LGG®	Infant formula for allergic babies (hydrolysed formula)	2009	powder