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INDUSTRY INVOLVEMENT IN ANTARCTIC BIOPROSPECTING

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Executive Summary

The focus of Antarctic research on its flora and fauna is very much on developing the knowledge base. Industries point to this situation as the reason for their limited focus on Antarctic organisms. Although they do express a general interest in samples, obtaining them does not form a central part of their strategy. Factors that were cited as limiting interest in Antarctica research by companies included: incomplete knowledge-base of Antarctic biodiversity, the current economic situation, lack of ownership of the samples, and uncertainty relating to intellectual property rights and commercial exploitation

Given the high risk and cost involved in pursuing this largely unexplored field, the number of companies involved in funding Antarctic research, screening samples and applying for Antarctic-based patents is restricted.

Some noteworthy discoveries based on Antarctic organisms and with potential commercial applications have been made in collaboration with industrial partners. However, it appears that none of these discoveries have led to commercialisation yet. Possibly the closest to commercialisation is the development of an anti-cancer drug involving an enzyme from Antarctica, which was isolated by the University of Cambridge, New Zealand, and is undergoing clinical testing by PharmaMar, a pharmaceutical company based in Spain. Recently, this work has stalled due to the companies' financial difficulties.

Arrangements between industrial and academic partners relating to the ownership of samples and to the sharing of potential benefits range from gentlemen's agreements foreseeing negotiations to this end once product development is imminent, to specific agreements on royalties and instalment payments made to the isolating institution. The role of the State whose claimed territory the sample was collected from is neither always clear, nor addressed. Ownership of the samples generally lies with the academic partner.

Patent applicants are largely pharmaceutical, chemical and food companies. Most patents are process, rather than product-based and centre around an isolate from an organism (frequently from the yeast *Candida antarctica*), rather than on a synthetic derivative.

Delays in the exchange of data and information have been attributed more to practical matters, such as insufficiently user-friendly databases, than due to patent restrictions or conscious withholding of information.

As a result of the above, industry, researchers and governments all stand to benefit if clear simple and practical rules governing the use of genetic resources in Antarctica were to be developed.

1 Introduction

This study follows up on the UNU/IAS Report “The International Regime on Bioprospecting: Existing Policies and Emerging Issues for Antarctica”, published in August 2003 and presented to the 26th session of the Antarctic Treaty Consultative Meeting (ATCM XXVI) as Information Paper 75. It is compiled in response to an ATCM decision to include the issue of biological prospecting activities on the preliminary agenda of its 27th session, to be convened in May 2004.

The 2003 UNU/IAS Report included a desktop review on the extent of bioprospecting, their commercial value and likely trends. It concluded that determining these issues will require a further survey of the relevant activities in Antarctica, the sectors using genetic material from Antarctica, research programmes most directly involved, and records of the appropriate patent offices. This study aims to answer some of these questions, in particular those relating to which sectors use Antarctic genetic material, and what indications records of patent offices give regarding these sectors’ focus on Antarctic-based commercialisation.

The present study was undertaken by drawing primarily on interviews with industry representatives and academics, as well as on records found in publicly-available patent databases. One clear limitation in researching the role of industry in any given subject matter is industry’s concern regarding confidentiality, and thus its frequent reluctance to share information that goes beyond promotional public knowledge. This constraint, evidenced by

several companies' refusal to speak about the subject matter, was dealt with by using as far as possible information made available by academics working with industry partners.

The next section will outline the information gained through the interviews. Subsequently, information relating to patents and patent applicants will be presented, before drawing some conclusions.

2 Industry's Interest: Interview Results

In the 2003 UNU/IAS Report, mention was made of Micromat, a public-private consortium whose aim was to conduct research into Antarctic microorganisms. Unlike deemed in the 2003 Report, such consortia are not frequent. Indeed, only one other comparable consortium, between the Australian-based pharmaceutical Cerylid Biosciences and the former Australian Antarctic Cooperative Research Centre (Antarctic CRC), has been identified. It is worthwhile to consider Micromat and the Antarctic CRC-pharmaceutical cooperation more closely, as it is conceivable that such collaboration agreements will become more attractive in the future.

Micromat, a project funded by the European Commission under its Fourth EU Framework Programme and running from 1999 to 2001, involved the Universities of Liège (Belgium), Ghent (Belgium), Bordeaux (France) and Nottingham (UK), the DSMZ (Germany), the British Antarctic Survey (UK), Merck Sharp & Dohme (Spain), Genencor International, and Biosearch – now Vicuron – (Italy). Its aim was to improve knowledge of the biodiversity of bacteria, protists and fungi in Antarctic microbial mats and to test this biodiversity for novel compounds of potential biotechnological use.¹ In accordance with the consortium agreement, the research institutions conducted the microbiotic work, while the industrial partners screened the purified strains for commercially interesting activities. Logistic support had been provided by Australia and, indirectly, by the US.

¹ <http://www.nerc-bas.ac.uk/public/mlsd/micromat/>

Merck Sharp & Dohme (Spain)

Merck Sharp & Dohme (Spain) is the name under which the US multinational pharmaceutical company Merck & Co operates in Spain. Merck & Co is a leading research-driven pharmaceutical company, whose human health products include medicines to help treat high blood pressure, osteoporosis and migraine. Worldwide sales in 2002 were over US\$21 billion. In 2002, Merck invested almost US\$2.7 billion in research and development. More than US\$18 billion have been invested in research and development over the past 10 years. Merck has over 64,000 employees.

According to Merck Sharp & Dohme (Spain), the strains were tested generally, rather than for specific purposes, and the work of the company was heavily restricted by its US lawyers on the grounds that they were not the owners of the strains.

Genencor International

Genencor International is one of the top 20 biotechnology companies, with US\$350 million in 2002 revenues and some 1,300 employees. From 1997-2001, Genencor International has invested approximately US\$232 million into research and development. It focuses on the bioproducts and health care markets, discovering and developing biochemicals for the industrial, consumer and agro-processing markets, and drugs targeting viral infectious diseases and cancer.

In contrast to Merck Sharp & Dohme, Genencor focused its screening activities on bacterial enzymes in particular, which had been isolated by Ghent University and the DSMZ. The bacterial enzymes were not the property of the industry according to the consortium agreement, but remain the property of the laboratory, which has isolated the bacteria. In the case of commercialisation, a provision, which remains active despite the project's termination, stipulates that the industry would have to consult both with the original isolators, and with the government whose sector the sample was taken from. Micromat represented Genencor's first activity with regard to Antarctic microorganisms. Thus, Genencor did not expect the work to lead to product development, but rather considered it as a learning phase. The bacteria, which remain in Genencor's culture collections, have been re-examined in the summer of 2003 as part of a short screening project. Although no commercially-exploitable activities were identified, the microorganisms are likely to be examined again when screening for another characteristic will be undertaken.

In contrast to Merck Sharp & Dohme, Genencor International did not highlight the constraints of its work imposed as a result of the lack of ownership of the genetic material, but instead underscored that the consortium provided it with a framework for obtaining interesting genetic samples in a legal manner. Another similar EU-funded project in China, which also involves collaboration with public and private partners, provides a similar opportunity to gain access to sample material. One problem identified with regard to working on Antarctic microorganisms is that they are difficult to grow and genetically very poorly characterised. The interviewee also pointed to the lag time between developing a sufficient knowledge base about an organism, and the commercial development on the basis of the organism. Thus, while Genencor is interested in Antarctic samples, it does not expect to conduct intense work on Antarctic microorganisms until the knowledge base on them is further developed. Moreover, given that industry's result-driven character, the interviewee said that Genencor would "never" pay for researchers to "just" study Antarctic microbes, as this is considered a purely academic exercise too costly to the private sector. Finally, the company's involvement could in future be limited if it involves negotiating for months whether, or how, it will obtain samples.

Vicuron Pharmaceuticals

Vicuron Pharmaceuticals is the result of a merger between Versicor Inc. and Biosearch Italia S.p.A, consummated in February 2003. Its lead products are in Phase III clinical trials and include an intravenous antibiotic for the treatment of serious Gram-positive infections. Commercialisation of its products is pending.

The third industrial partner, Vicuron Pharmaceuticals (formerly Biosearch), explained that its focus in this project was on strains able to produce anti-freeze molecules or activities. In the search for anti-infective strains, some microorganisms were submitted to secondary tests. These showed, however, that the microorganisms had low activity-levels, known active molecules, or that they were toxic to mammalian cells. Such findings are usual, and illustrate the low success rate in screening. Like Genencor, Vicuron highlighted the advantage of collaboration agreements for the purposes of obtaining microbial strains, and noted that the company management would not fund employers to collect samples in Antarctica. The interviewee noted that although Vicuron has a general interest for setting up collaboration

agreements to obtain Antarctic strains, currently this is not being pursued because the company has sufficient strains from other parts of the world to screen.

Micromat coordinator Annick Wilmotte from **Liège University** (Belgium) explained that the arrangement with Australia was that data collected on the basis of the samples would be made available to all partners through a database. However, due to the fact that the database was insufficiently user-friendly, delays in this commitment occurred. She noted that the consortium agreement included one paragraph relating to intellectual property right, which stipulates that in the case of an industrial application, negotiations would be held involving all Parties, including the relevant Claimant State (in this case, Australia). However, it has not come to this, yet. Her interpretation of industry's interest in Antarctic microorganisms is that it is high, but lack of funding prevents fully pursuing these interests. She also explained that under the 6th European Framework Programme little hope exists for similar projects as the guidelines foresee consortia with a significantly larger number of participants, an aspect that would make it more difficult to reach agreement on as difficult and complex an issue as intellectual property rights.

Dominic Hodgson, **British Antarctic Survey**, explained that under Micromat, industry screened 3,500 organisms, but that it would take some 8-10 years between research on these organisms and products entering the market because:

- the knowledge base remains to be fully developed
- present products have to be proven to be inadequate
- a “gap” in the market place must become available

Confirming statements made by industry, he noted that companies are generally interested in obtaining Antarctic microorganisms, but are not willing to make significant financial investments to this end. He explained that Antarctic microorganisms still have a relatively small profit margin, with no major results obtained yet. According to his interpretation, biological prospecting activities have not in fact been increasing, but rather the awareness of such activities and the drive under the Antarctic Treaty System to manage these activities have increased. He also noted that technological improvements are underway, with companies being able to screen larger amounts of samples in less time.

David Nichols, formerly with the Antarctic CRC and now at the **University of Tasmania**, Australia, said the Antarctic CRC had had a commercial agreement between 1995 and 2002 with the Australian pharmaceutical company Cerylid Ltd concerning the isolation and provision of Antarctic bacteria isolated from, primarily, Antarctic soil samples. He said the commercial partner's screening of the isolates for human pharmaceuticals is ongoing, and might involve sharing the isolates with another company to further advance the screening process. The agreement contains a provision according to which royalties will flow back to the Antarctic CRC or its members. Regarding the isolates' ownership, the agreement provided that the pharmaceutical company did not own them, but that they were provided for a limited time period for a specific task, following which ownership would go back to the Antarctic CRC. He said such public-private partnerships for isolates screening are relatively rare. He noted that there is a slow shift in focus from thermophilic to cold-active enzymes.

Michael Danson from **Bath University** (UK) has conducted Antarctic bioprospecting activities that were funded to 50% by the British Research Council, and to 50% by Glaxo Smith Kline, Reckitt Benckiser, and Veridian Enviro Solutions. He said the companies expressed concern about legal issues surrounding this work, as they were reluctant to invest into developing enzymes if they were to find that they could not exploit them. The agreement reached was no more than a gentleman's agreement, according to which an agreement, involving royalties going back to Waikato University, the supplier of the organisms, would be reached before exploitation would start.

Reckitt-Benckiser (UK)

With some 22,300 employees and over US\$3,500 million in 2002 sales, Reckitt-Benckieser is a leading player in the market for household cleaning products. It also produces over-the-counter pharmaceuticals, including analgesics, antiseptics, flu remedies and gastrointestinal medications.

Reckitt-Benckiser (UK) said that extremophiles are of general interest to the industry, but must not necessarily originate from Antarctica. As such, Antarctic research is not at the forefront of its strategy, as opposed to in 2001 when it supported Michael Danson's work. No specific reason is attributable to this change in strategy, which changes frequently and rapidly due to the company's result-driven focus. The interviewee noted that the drawback

of Antarctic projects include their long-term character, high risk and high cost; and explained that the agreement reached with the two other industrial partners and Danson are confidential and thus details of property ownership and commercialisation agreements cannot be disclosed.

Unilever (UK)

Unilever is one of the world's leading suppliers of consumer goods in foods, household and personal care product. Unilever UK has 12,000 employees and annual UK sales of over £2,5 billion. Over 5 years up to 2006, Unilever UK is investing £13 million in the Unilever Centre for Molecular Informatics, a partnership with Cambridge University's chemistry department.

Unilever (UK) said it had started working on Antarctic microorganisms in the 1980s with several universities in, amongst others, the UK, Norway, and the US. This effort has been discontinued, however, as the work remains largely pre-commercial and pre-exploitative.

Nicholas Russell from **Imperial College London** (UK) outlined a European-funded project called "Coldzyme", whose main industrial partner was Unilever (The Netherlands) and whose aim was to identify and describe bacteria with cold-active enzymes. Under the project, cultures were collected, bacteria catalogued and preliminary research conducted on enzymes. Funding was discontinued when the project entered its second phase to investigate potential applications of the enzymes. The reasons for this remain unclear. He said industry's funding of Antarctic research has been low due to the fact that they cannot claim ownership of the Antarctic microorganisms, and mentioned that colleagues have discontinued cooperation with some industries as these had insisted on claiming ownership of the microorganism studied. He said that industry is waiting for more basic research before dealing with Antarctic microorganisms more intensively. He noted that while no Antarctic-based product or process has been commercialised to date, and it therefore remains to be seen how ownership issues will be solved, the fact that the microorganisms are usually genetically modified for this purpose may support the argument that the product or process is not "Antarctic-based" as such. He questioned whether Antarctic bioprospecting activities themselves have increased over the past decade.

Jim Raymond from **Nevada University** (US), engaged in research on algal-based anti-freeze proteins, explained that the fish-based anti-freeze protein had a lot of promise but has so far failed to give rise to any specific products. He said much interest around this issue is present, but a lot of basic research remains to be done, and noted that fish anti-freezes can be obtained either by harvesting fish, which is wasteful, or by transposing the relevant genes into bacteria and cultivate them, which is relatively costly. He said that Unilever had expressed interest in these proteins (Unilever, however, did not confirm this). According to his knowledge, not product or process based on Antarctic microorganisms has been commercialised yet. He noted that Nevada University does not have any type of agreement with another institution/country regarding its anti-freeze research as the algae in question are not endemic to the Antarctic environment and could be collected from other parts of the world if restrictions were imposed on their collection in Antarctica.

David Saul from the **University of Auckland** (New Zealand) said that the thermophilic enzyme, isolated 15 years ago from an organism found in a volcanic vent in Mount Erebus, is expected to be commercialised for forensic work. The enzyme has unusually high levels of activity of extracting DNA from forensic material. Interest in the enzyme has been expressed by many forensic institutions scientists, the Australian Department of Justice and the Crown Prosecutor of the Northern Territory, Australia. Current negotiations with Antarctica New Zealand are to reveal whether they will demand royalties on any potential commercial success. (Details about the negotiations were not obtained). He noted that the enzyme in question is very similar to others from extremely hot environments, and said that the difficulty with cold-loving organisms is that their genes, when transposed into a medium-temperature organism, often fail. Regarding potential restrictions on Antarctic bioprospecting activities, he said that given the vast microbial flora in any site around the world, researchers would simply go elsewhere. However, he noted that a restriction may not be necessary given that much bioprospecting is being undertaken as part of other research projects.

Murray Munro from the **University of Canterbury** (New Zealand) explained that PharmaMar (Spain) started funding the University's Antarctic bioprospecting work some 12 years ago. The research led to the isolation of variolin from an Antarctic sponge, synthetic

derivatives of variolin were developed and patented by PharmaMar, and are now being developed as an anti-cancer drug. Currently, the derivatives are being tested *in vivo*, which in terms of drug development means that about 50% of the work has been completed. The University of Canterbury's agreement with PharmaMar foresees that royalties of any commercial products will be paid, and also provides for milestone payment. Figures and further details are confidential. He noted that PharmaMar's current financial difficulties have led to the stalling of any further work.

PharmaMar is Spain's main biopharmaceutical company, focusing on research and development of anti-tumour compounds from marine organisms.

3 Patents

A patent database search, which is not deemed exhaustive but indicative of existing patents, has revealed the following information. Companies applying for patents include:

Bayer AG (Germany): produces health care and agricultural products, chemicals and polymers. Its 2002 sales were over €29,000 million, and its 2002 research and development expenses amounted to €2,500 million. Bayer employs over 118,000 people, of which 12,000 work in research and development.

Henkel KGAA (Germany): operates *inter alia* in laundry and home care, cosmetics and toiletries, and consumer and craftsmen adhesives. Its 2002 sales amounted to €9,656 million, and its 2002 research expenditures amounted to €259 million. It counts some 500,000 employees, of which around 3,000 are engaged in research, product development and application engineering.

SmithKline Beecham: SmithKline Beecham merged with Glaxo Welcome in 2000 to form GlaxoSmithKline (GSK). GSK is a leading research-based pharmaceutical company focusing, *inter alia*, on anti-infectives, drugs for the Central Nervous System, respiratory system and gastro-intestinal/metabolic system, over-the-counter medicines and oral care products. Based on 2002 annual results, the company had sales of US\$31.8 billion, with new products representing 27% of its total pharmaceutical sales (US\$27 billion). Its research & development budgets amounts to US\$4 billion. Of its 100,000 employees, 16,000 work in research and development.

Astra: Astra merged with Zeneca plc in 1999 to create AstraZeneca. AstraZeneca is a leading pharmaceutical company developing medicines against cancer, cardiovascular and gastrointestinal problems, infections and respiratory problems. In 2002, its sales totaled US\$17,8 billion and expenditures for research and development amounted to US\$3,1 billion. It has 58,000 employees, of which 11,000 work in research and development.

Novonordisk (Denmark): a healthcare company and world leader in diabetes care, also focuses on growth hormone therapy and hormone replacement therapy. Its net 2002 turnover amounted to some US\$4,200 million. Of its roughly 18,600 employees, 19% work in research and development.

Du Pont (US): a science company focusing on food and nutrition, health care, apparel, security, construction, electronics and transport. Its 2003 revenues amounted to US\$27 billion. 1,500 of its 78,000 employees work in research and development.

Chisso Corporation (Japan): a chemical company producing fertilisers, PVC, plasticisers, polypropylene, synthetic fibres and fine chemicals. It employs over 1,900 people.

Loders Croklaan (The Netherlands): a leading producer of speciality oils and fats for the food and health industries. It is part of the IOI Group, a Malaysian company whose core business is the cultivation of oil palm and rubber.

Haarmann & Reimer GmbH (Germany): a producer of synthetic flavours and fragrances. In 2003 it merged with DRAGOCO to form Symrise. Symrise, which produces flavours, fragrances, aroma chemicals and cosmetics, invests 8% of its sales into research and development. Its 2002 sales totalled €1,246 million. Some 200 of its 6,000 employees work in research and development.

Unilever (UK): one of the world's leading suppliers of consumer goods in foods, household and personal care product. Unilever UK has 12,000 employees and annual UK sales of over £2,5 billion. Over 5 years up to 2006, Unilever UK is investing £13 million in the Unilever Centre for Molecular Informatics, a partnership with Cambridge University's chemistry department.

Lysi HF (Iceland): creates products based on marine lipids, including children's cod liver oil, oil used as feed ingredient in aquaculture and squalane, a transparent odourless oil used mainly in the cosmetics industry.

DSM NV (The Netherlands): produces biotechnological and chemical products, with pharmaceuticals recently having become its biggest end-use market. DSM also produces

food specialities and bakery ingredients. Its 2002 net sales amounted to €5,636 million. It invests around 5% of its annual turnover in research and development, and has over 18,000 employees.

Jujo Paper Co Ltd (Japan): Jujo Paper merged with Sanyo-Kokusaku Pulp in 1993 to form Nippon Paper Industries. Nippon Paper Industries produces *inter alia*, writing, packaging and industrial papers, as well as newsprint. It employs over 6,500 people

Mitsubishi Gas Chemical Company Inc (Japan): produces, *inter alia*, petroleum-derived chemicals, fertilisers, synthetic resin, dyes, pharmaceutical products, food additives and detergents. It employs some 2,500 people.

Higashimaru Shoyu Company Ltd (Japan): manufactures soy sauce. Information on Higashimaru Shoyu is available only in Japanese.

Tokuyama Corporation (Japan): a chemical company producing, *inter alia*, low heat cement, pharmaceutical and agricultural chemical intermediates and moisture absorbents. Its 2003 net sales amounted to US\$1,88 billion, and its 2003 research and development expenditures totalled US\$64, 829. Of its 4,500 employees, about 500 work in research and development.

Lion Corporation (Japan): produces pharmaceuticals, chemicals, food, beauty care, oral care and domestic products. Its 2002 consolidated sales amounted to about US\$2,900 million, and its 2002 research and development expenditures totalled US\$75 million. Lion Corporation employs some 5,500 people.

Nippon Soda Company Ltd (Japan): produces chemicals, agricultural products and pharmaceuticals. Its 2002 net sales totalled US\$1,04 billion, and its research and development expenditures amounted to around US\$51 million (nearly 4% of the consolidated net sales). Nippon Soda employs over 1,500 employees.

The above information shows that a total of 18 companies have applied for Antarctic-based patents, whereby most applicants are Japanese-based companies, followed by German ones (See Figure 1).

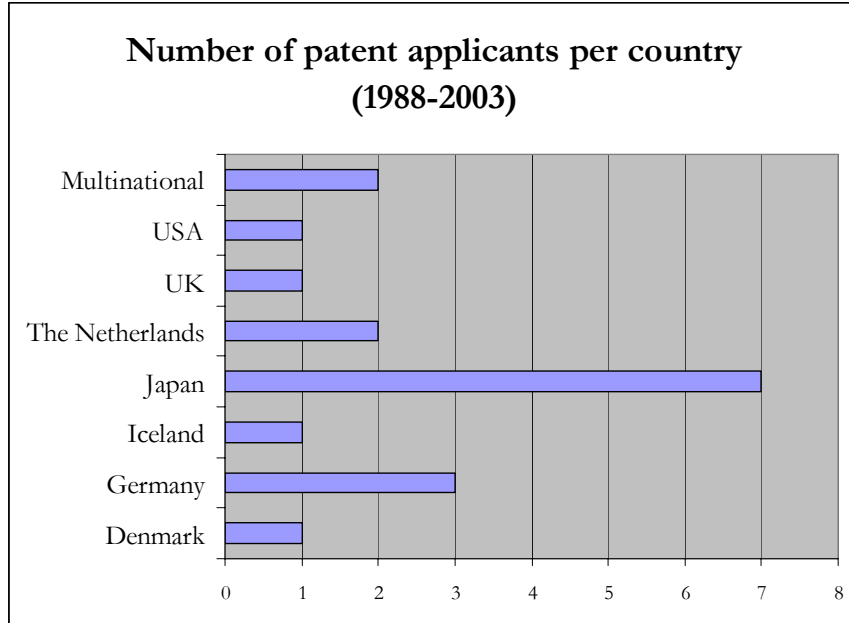


Figure 1: Number of patent applicants per country (1988-2003)

The patents examined indicate a recent decrease in patents granted. Thus, between 2002 and 2003, 6 patents were issued, whereas 10 patents were granted between 1996 and 1997. Prior to this, fewer patents were granted, with one being issued between 1990 and 1991 (See Figure 2).

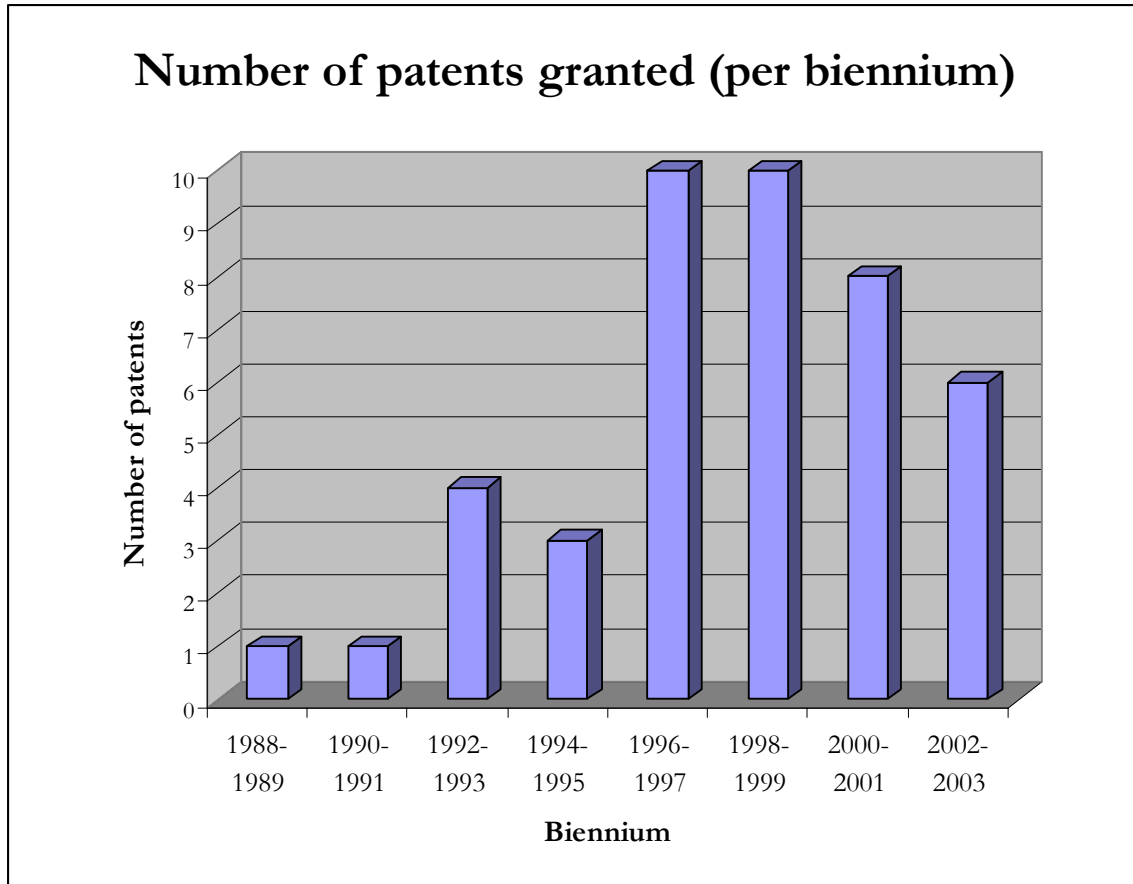


Figure 2: Number of patents granted (per biennium)

Most patents filed are process- rather than product-based, with many relating to the yeast *Candida antarctica*. The distinction between process- and product-based patents is determined by whether the invention relates to a product or to a process.

Candida antarctica

Candida antarctica, one of 154 species of the genus *Candida*, belongs to the Phylum Ascomycota and to the Class Ascomycetes. It is an alkali-tolerant yeast found in the sediment of Lake Vanda, Antarctica. Two lipase variants from *Candida antarctica*, lipase A and B, have proven of particular interest to researchers (lipase being enzymes that break down fats).

Examples of process-based patents relate to:

- the preparation of optically active amines, which are prepared in the presence of lipase from the Antarctic yeast *Candida antarctica*. The amines can be used as intermediates for preparing pharmaceuticals and crop protection agents (US6387692)
- the preparation of esters in the presence of *Candida antarctica* lipase A, or a variant thereof. The esters are useful as ingredients in fat blends such as margarine (WO0153511)
- the enzymatic synthesis of polyesters in the presence of a lipase derived from, amongst others, *Candida antarctica*. The polyesters are useful in formulating products such as skin creams and cosmetics as they normally function as thickeners or softeners in such formulations (US5962624)
- the enzymatic resolution of certain esters, using *Candida antarctica* lipase fraction B as enzyme catalyst. The products of this invention are useful as precursors for chemicals of high value in the agricultural and pharmaceutical industry (US5928933)
- the preparation of a certain acid ethyl ester with lipase from *Candida antarctica*. The ester is the flavouring that is the character impact compound of William pears. Unlike according to the invented process, the old way of preparing the ester did not result in it being a natural substance in the context of food law and therefore could not be called a natural aroma substance (US5753473)
- the preparation of a triglyceride in the presence of a mixture of lipase A and lipase B obtained from *Candida antarctica*. The triglycerides have beneficial medical effects (US5604119)
- the preparation of an optically active ester using an enzyme originating from *Candida antarctica*. The ester can be used for preparing pharmaceuticals such as benzothiazepines and benzazepines (US5407828)
- the immobilisation of thermostable microbial lipase, preferably from *Candida antarctica*. The immobilised lipase can be used for hydrolysis of fats (US5342768)
- the hydrolysis of water-insoluble ester in the presence of a lipase derived from a strain of *Candida antarctica*. The ester hydrolysis can be applied to hydrolysis of resin

- ester. This is useful as some types of pulp made from wood have high resin content, and the resin can create disturbances in the process of pulp manufacture and may have negative effects on the properties of the final pulp product (WO9218638)
- the production of optically active carboxylic acid in the presence of *Candida antarctica* or lipase originated there from. The carboxylic acid is useful as an intermediate for producing industrial chemicals, agrochemicals or medical agents (JP2003144190)
 - the decomposing of soy sauce oil with the yeast *Candida antarctica* T-24 in order to generate soy sauce oil as a by-product in a soy sauce brewing method (JP2002101847)
 - the production of a specific polymer not containing a metal atom in the presence of a lipase originating from *Candida antarctica*. The polymer can be useful for medical equipment (JP2000044658)
 - the production of a particular furanone compound in the presence of a lipase from *Candida antarctica*. The compound has a sweet fruity fragrance and can be useful as food perfume (JP10084988)
 - the production of an optically active compound in the presence of a hydrolase originating from fungi such as a lipase from *Candida antarctica*. The compound is useful as a synthetic intermediate for medicines and agrochemicals (JP7115992)
 - the use of a glycoprotein produced by *Pseudoalteromonas antarctica* in the preparation of pharmaceutical, veterinary and cosmetic compositions for topical or mucosal application aimed at the treatment and re-epithelialisation of wounds (WO02102406)
 - the use of an extract from the green alga *Prasiola crispa* spp. Antarctica for cosmetic skin treatment, care or protection, including as sun protector and after-sun cream (WO0238121)

Product-based patents relate to:

- the development of frozen confectionary products, such as ice cream, comprising one or more anti-freeze proteins derived from plants, including from the Antarctic-based *Nothofagus antarctica*, *Deschampsia antarctica* and *Umbilicaria antarctica*. The anti-

- freeze proteins inhibit ice recrystallisation and thus provide a good texture to frozen confectionary product (GB19970014412)
- the development of a *Candida antarctica* lipase A and a variant thereof, which can be used as a detergent enzyme or digestive enzyme, or to avoid pitch trouble arising *inter alia* in processes for preparing mechanical pulp in paper-making processes using mechanical pulp (US6074863)
 - a glycoprotein obtained by culture of the bacterial species *Pseudoalteromonas antarctica* CECT4664, which is useful for coating liposomes in order to improve their stability in relation to external factors such as surfactants (WO9842731)
 - a thermally stable lipase native to *Candida antarctica*, to be used for processing high-melting substrates at 60°C for, *inter alia*, the randomisation of fat in the margarine industry (US5273898)
 - the production of a particular stimulating agent containing the extract of an alga belonging to the genus *Durvillea*, including *Durvillea antarctica*. The stimulating agent prevents the development of skin wrinkles (JP9176036)

The above shows that sectors where patents have potential applications include the pharmaceutical, agriculture, food, cosmetics and chemistry sectors (See Figure 3).

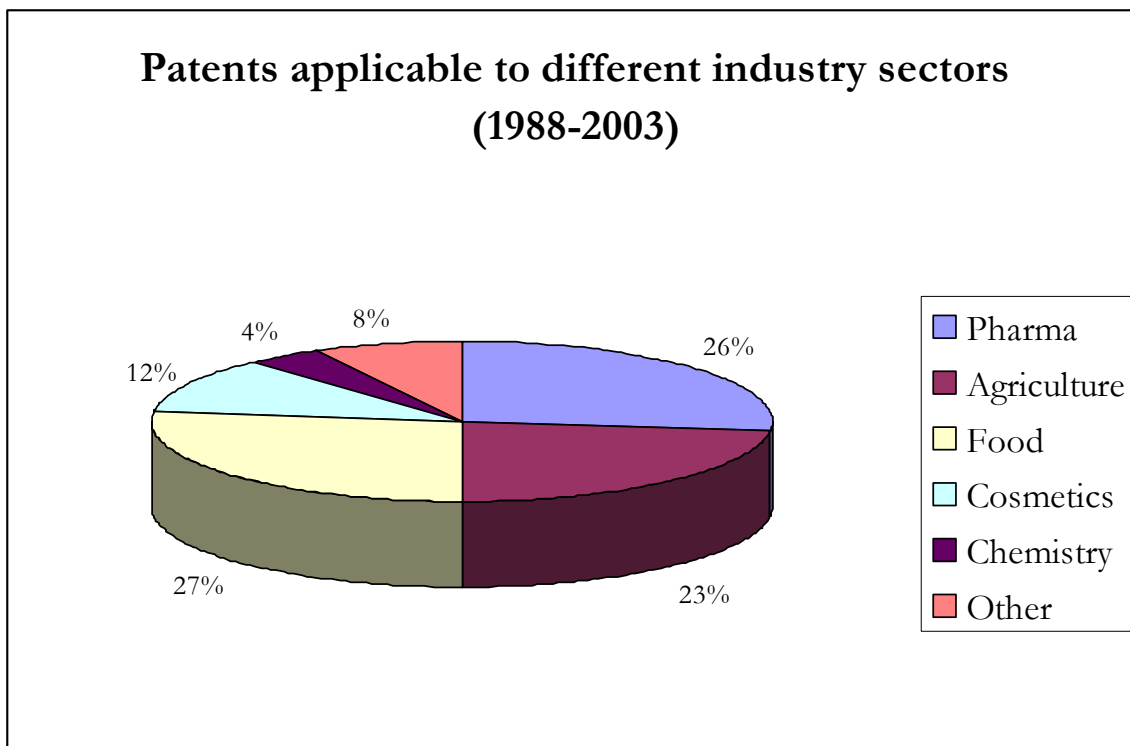


Figure 3: Patents applicable to different industry sectors (1988-2003)

4 Conclusion

This study has shown that while products or processes based on Antarctic organisms have not yet been commercialised, the scope for such a development exists. Not only do some Antarctic extremophiles exhibit potentially exploitable characteristics, but industry has also displayed an interest in screening these organisms. Restrained by the incomplete knowledge-base of Antarctic biodiversity and the current economic situation, companies have not made it a priority to focus their attention on Antarctic samples, as the cost, risk and time involved do not concur with the necessity to generate marketable products.

The number of patents issued appears to support the interpretation that, following a period of greater anticipation in face of the opening of a new “frontier”, companies have reduced the intensity of their involvement in the light of the yet-to-be developed knowledge base. In

addition, lack of ownership of the samples, and uncertainty relating to intellectual property rights and commercial exploitation are likely to have acted as disincentives.

Given that the largest part of inventions are of relevance to the pharmaceutical industry, a breakthrough commercialisation can be expected to attract a significant amount of publicity and thus, revived interest by companies. Moreover, since rules regarding access, sample ownership, benefit-sharing and intellectual property rights would provide certainty to both academic researchers and industries, they may be favourable disposed towards attempts to address the absence of such rules.

The data used in this study does not give a clear indication of the different roles assumed by claimant and non-claimant States.

Factors that seem to influence a company's interest in Antarctic samples are not only its financial situation, but also its focus on research and development, as well as its existing expertise in working with extremophiles. If bioprospecting is to continue in a similar form as it has up to date, i.e. as part of wider research projects and with the sampling being undertaken by academic researchers, it should be in the interest of the international community as a whole to develop a framework under which the commitments of the Antarctic Treaty are honoured, and the opportunity for developing necessary products or processes maintained.

ANNEX: PATENT DETAILS

Method for producing optically active s-6-hydroxy-2,5,7,8- tetramethylcumarone-2-carboxylic acid

Inventor: Tamura Yutaka

Applicant: Mitsubishi Gas Chem Co Inc

Publication info: **JP2003144190** - 2003-05-20

Use of glycoprotein for the treatment and re-epithelialisation of wounds

Inventor: Casaroli Marano Ricardo (Es); Garces Garces Josep (Es); (+5)

Applicant: Casaroli Marano Ricardo (Es); Garces Garces Josep (Es); (+6)

EC: A61K38/46; A61K38/22

IPC: A61K38/46 ; A61P17/12

Publication info: **WO02102406** - 2002-12-27

Cosmetic skin treatment, care or protection composition

Inventor: Hoyer Kirsten (De); Karsten Ulf (De); (+2)

Applicant: Henkel KGAA (De); Hoyer Kirsten (De); (+3)

EC: A61K7/42T; A61K8/97C; (+2)

IPC: A61K7/48 ; A61K35/80 ; (+1)

Publication info: **WO0238121** - 2002-05-16

Cryophilic enzyme-producing mold

Inventor: Murayama Ryuji; Kanefuji Gakuo; (+2)

Applicant: Nagata Sangyo KK

Publication info: **JP2002262859** - 2002-09-17

Method for treating soy sauce oil

Inventor: Furubayashi Makio; Nakahara Tadaatsu; (+3)

Applicant: Higashimaru Shoyu Co Ltd

Publication info: **JP2002101847** - 2002-04-09

Process for the preparation of optically active amines

Inventor: Stelzer Uwe (De); Dreisbach Claus (De)

Applicant: Bayer AG (DE)

EC: C07C235/06; C12P41/00D2

IPC: C12P41/00

Publication info: **US6387692** - 2002-05-14

Degradation of biologically degradable polymers using lipase from *Candida antarctica* and a cutinase

Inventor: Koch Rainhard; Lund Henrik

Applicant: Bayer AG

IPC: C12P1/00 ; C12P7/62

Publication info: **NZ337239** - 2001-09-28

Process for preparing esters

Inventor: Christensen Morten Wuertz (dk); Borch Kim (dk)
Applicant: Christensen Morten Wuertz (dk); Borch Kim (dk) (+1)
EC: C12P33/00; C12P7/62
IPC: C12P7/62
Publication info: **WO0153511** - 2001-07-26

Enzymatic resolution of benzodiazepine-acetic acid esters (3-oxo-2,3,4,5-1H-tetrahydro-1,4-benzodiazepine-2-acetic acid) with a lipase from *Candida antarctica*

Inventor: Wells Andrew Stephen
Applicant: Smithkline Beecham p
IPC: C12P41/00 ; C12P17/16 ; (+2)
Publication info: **NZ336376** - 2000-11-24

Process for obtaining fatty esters of diacetyltartaric acid using biocatalysts

Inventor: Garcia Martin Tomas (Es); Martinez Rodriguez Mercedes (Es); (+2)
Applicant: Univ Madrid Complutense (Es)
IPC: C12P7/62
Publication info: **ES2146162** - 2000-07-16

Process for obtaining enantiomerically enriched N-acylazetidine-2-carboxylic acids comprising the biotransformation of racemic N-acylazetidine-2-carboxylic acid ester with an enantiospecific enzyme

Inventor: Parratt Julian Simon; Taylor Stephen John Clifford
Applicant: Astra AB
IPC: C12P41/00 ; C12P17/10 ; (+1)
Publication info: **NZ333445** - 2000-06-23

C. antarctica lipase variants

Inventor: Egel-Mitani Michi (Dk); Hansen Mogens Trier (Dk); (+4)
Applicant: Novonordisk As (Dk)
EC: C12N9/20; D21H21/02
IPC: C12N9/20 ; C12N15/63 ; (+2)
Publication info: **US6074863** - 2000-06-13

Para-dioxanone-based polymer

Inventor: Nishida Haruo; Yamashita Mitsuhiro
Applicant: Tokuyama Corp
Publication info: **JP2000044658** - 2000-02-15

C. antarctica lipase and lipase variants

Inventor: Egel-Mitani Michi (Dk); Hansen Mogens Trier (Dk); (+4)
Applicant: Novonordisk As (Dk)
EC: C12N9/20; D21H21/02
IPC: C12N9/20 ; C12N15/63 ; (+2)
Publication info: **US6020180** - 2000-02-01

Enzymatic synthesis of polyesters

Inventor: Hill Karlheinz (De); Lagarden Martin (De); (+3)

Applicant: Hendel Kommanditgesellschaft A (De)

EC: C08G63/81; C08G63/87; (+1)

IPC: C08G63/78 ; C12N9/00

Publication info: US5962624 - 1999-10-05

Process for the enzymatic resolution of N-(alkoxycarbonyl)-4-ketoproline alkyl esters or N-(alkoxycarbonyl)-4-hydroxyproline alkyl esters using *Candida antarctica* lipase B

Inventor: Hong Wonpyo (US); Dicosimo Robert (US)

Applicant: Du Pont (US)

EC: C12P13/24; C12P13/04; (+1)

IPC: C07C1/04 ; C12P13/24

Publication info: US5928933 - 1999-07-27

Solvent-free method for reacting short-chain alcohols and acids using *C. antarctica* lipase immobilized to acrylic resin

Inventor: Cho Nam Ryun (Kr); Hwang Soon Ook (Kr); (+1)

Applicant: Yukong Ltd (Kr)

EC: C12P7/62

IPC: C12P7/62 ; C12P7/64

Publication info: US5908769 - 1999-06-01

A method for producing an optically active 2-alkanol

Inventor: Yano Hitoshi (Jp); Yoshida Naoyuki (Jp)

Applicant: Chisso Corp (Jp)

EC: C12P41/00C2; C12P7/62

IPC: C12P7/04 ; C12P7/62

Publication info: EP0908522 - 1999-04-14

Glycoprotein for the protection of liposomes

Inventor: Bozal De Febrer Nuria (Es); De La Maza Ribera Alfonso (Es); (+6)

Applicant: Bozal De Febrer Nuria (Es); Mercade Gil Maria Elena (Es); (+7)

EC: C07K14/195; A61K9/127B; (+1)

IPC: C07K2/00 ; C07K14/195 ; (+3)

Publication info: WO9842731 - 1998-10-01

Immobilized lipases on a dry, porous particulate hydrophobic support and containing a non-ionic surfactant

Inventor: Bosley John Anthony (GB); Moore Stephen Raymond (GB)

Applicant: Loders Crokiaan Bv (Nl)

EC: C12N11/08; C12N11/14

IPC: C12P7/64 ; C12N11/14 ; (+2)

Publication info: US5773266 - 1998-06-30

Process for the preparation of trans-2, cis-4-decadienoic acid ethyl ester

Inventor: Gatfield Ian (De); Kindel Guenter (De)

Applicant: Haarmann & Reimer Gmbh (De)

EC: C12P7/62

IPC: C12P7/62

Publication info: US5753473 - 1998-05-19

Production of (d)-3(2h)-furanone compounds

Inventor: Suzuki Akio; Nozaki Michio

Applicant: Takasago Internatl Corp

Publication info: JP10084988 - 1998-04-07

Acylaytion by enzyme

Inventor: Orsat Bernard; Spurr Paul; (+1)

Applicant: F Hoffmann La Roche AG

Publication info: JP10036301 - 1998-02-10

Plant antifreeze proteins for use in frozen confectionary

Publication date: 1998-02-11

Inventors: Byass Louise Jane; Darling Donald Frank; Doucet Charlotte Juliette; Fenn Richard Anthony; Lillford Peter John; McArthur Andrew John; Needham David; Sidebottom Christopher Michael; Smallwood Keith; Smallwood Margaret Felicia

Applicant: Unilever PLC (GB)

Application Number: GB19970014412 19970708

Priority Numbers: EP19960305497 19960726; EP19960305499 19960726; EP19960308362 19960726; EP19970301719 19960726; EP19970301733 19960726

IPC Classification: C07K14/415 ; A23G9/00 ; A23L3/36

Agent for biologically stimulating synthesis of hyaluronic acid

Inventor: Miyahara Tsuneo; Ehata Shinya; (+1)

Applicant: Lion Corp

Publication info: JP9176036 - 1997-07-08

Enantiomeric separation of (RS)1-(4-chlorophenyl)-2-chloroethanol by lipase catalyzed hydrolysis of its acetate

Inventor: Zard Lydia (Fr); Tixidre Arlette (Fr)

Applicant: Synthelabo (Fr)

EC: C12P41/00C2; C07C31/36; (+3)

IPC: C12P41/00

Publication info: US5677168 - 1997-10-14

Process for the esterification of carboxylic acids with tertiary alcohols using a lipase from *Candida antarctica*

Inventor: Bosley John Anthony (GB); Casey John (GB); (+2)

Applicant: Unichem Chemie Bv (NL)

EC: C12P7/62

IPC: C12P7/62

Publication info: US5658769 - 1997-08-19

Method of producing optically active amines

Inventor: Stelzer Uwe (De); Dreisbach Claus (De)

Applicant: Bayer AG (De)

IPC: C12P13/00 ; C12P41/00

Publication info: CA2244917 - 1997-08-07

Verfahren zur Herstellung von optisch aktiven Aminen

Inventor: Dreisbach Claus Dipl Chem Dr (De); Stelzer Uwe Dipl Chem Dr (De)

Applicant: Bayer AG (DE)

EC: C12P41/00D2; C07C209/88

IPC: C12P41/00 ; C12P13/02 ; (+7)

Publication info: DE19603575 - 1997-08-07

Biocatalytic process for obtaining optically pure enantiomers of Flurbiprofen

Inventor: Nicolosi Giovanni; Patti Angela; (+2)

Applicant: Consiglio Nazionale Ricerche

IPC: C07C

Publication info: IT1274482 - 1997-07-17

(+)-6-(5-chloropyrid-2-yl)-7-oxo-vinyloxycarbonyloxy-5,6- dihydropyrrole (3,4b) pyrazine and its use in a process for the preparation of (+)-6-(5-chloropyrid-2-yl)-5-(4- methylpiperazin-1-yl)-carbonyloxy-7-oxo-5,6- dihydropyrrole (3,4b) pyrazine

Inventor: Garcia Campos Roberto (Es); Linares Lopez Francisco J (Es); (+3)

Applicant: Astupaharma S A (Es)

IPC: C07D487/04 ; C07B57/00 ; (+1)

Publication info: ES2101653 - 1997-07-01

Process for producing triglycerides from glycerol and long-chain polyunsaturated fatty acids using lipase from *Candida antarctica*

Inventor: Haraldsson Gudmundur G (Is); Svanholm Hanne (Dk); (+1)

Applicant: Novonordisk As (Dk); Lysi Hf (Is)

EC: C11C3/04; C12P7/64; (+1)

IPC: C12P7/64

Publication info: US5604119 - 1997-02-18

Resolution of (RS)-ibuprofen by *Candida antarctica* catalyzed esterification with long chain alcohols while removing water

Inventor: Trani Michael (Ca); Ergan Fran Oise (Fr); (+1)

Applicant: Canada Nat Res Council (Ca)

EC: C07C51/493; C12P7/22; (+3)

IPC: C07C15/02

Publication info: US5561057 - 1996-10-01

Production of organic dicarboxylic acid diester

Inventor: Iwasaki Ryozi;Uno Akinori; (+1)

Applicant: Lion Corp

Publication info: JP8154690 - 1996-06-18

Process for stereoselection of (2R,3S)-3-phenylglycidic ester using lipase from *Candida antarctica*

Inventor: Kierkels Joannes G T (NL); Peeters Wijnand P H (NL)

Applicant: DSM NV (NL)

EC: C07D303/48; C12P41/00C4; (+1)

IPC: C12P41/00 ; C12N1/16

Publication info: US5407828 - 1995-04-18

Enzymatic production of optically active compound

Inventor: Takagi Naoyuki; Others: 04

Applicant: Nippon Soda Co Ltd

Publication info: JP7115992 - 1995-05-09

Immobilization of thermostable microbial lipase by adsorption to macroporous inorganic carrier particles

Inventor: Pedersen Sven (Dk); Hansen Tomas T (Dk)

Applicant: Novonordisk AS (DK)

EC: C12N11/14; C12N9/20

IPC: C12P7/64 ; C12P7/62 ; (+1)

Publication info: US5342768 - 1994-08-30

Thermally stable and positionally non-specific lipase isolated from *Candida*

Inventor: Ishii Michiyo (Jp)

Applicant: Noro Nordisk A S (DK)

EC: C12N9/20; C12N11/02

IPC: C12P7/64 ; C12N9/20 ; (+1)

Publication info: US5273898 - 1993-12-28

Powder emulsifier composition for food

Inventor: Oshima Motomu; Others: 03

Applicant: Lion Corp

Publication info: JP5236886 - 1993-09-17

Lipase-catalyzed ester hydrolysis

Inventor: Heldt-Hansen Hans Peter (Dk); Awaji Haruo (Jp); (+3)

Applicant: Novonordisk AS (Dk); Jujo Paper Co Ltd (Jp)

EC: C12P7/64; D21C5/00B; (+1)

IPC: C12P7/64 ; D21C3/00

Publication info: WO9218638 - 1992-10-29

Immobilization of lipase by adsorption on a particulate macroporous resin

Inventor: Eigtved Peter (Dk)

Applicant: Novonordisk AS (DK)

EC: C12N9/20; C12N11/02; (+1)

IPC: C12N11/08 ; C12P7/62 ; (+1)

Publication info: US5156963 - 1992-10-20

Immobilized lipase preparation and use thereof for ester synthesis

Inventor: Pedersen Sven (Dk); Eigtved Peter (Dk)

Applicant: Novonordisk AS (DK)

EC: C12N11/08

IPC: C12N11/08 ; C12P7/62

Publication info: **WO9015868** - 1990-12-27

Heat sensitive bacterial alkaline phosphatase

Inventor: Kobori Hiromi (Jp); Shizuya Hiroaki (US); (+1)

Applicant: Kobori Hiromi (Jp); Shizuya Hiroaki (US); (+1)

EC: C12N9/16; C12Q1/42

IPC: C12N9/16 ; C12Q1/42 ; (+1)

Publication info: **US4720458** - 1988-01-19