CASE STUDY ON BIOTECH INNOVATION SYSTEMS

NORWAY

Vol. 2: Marine biotechnology.

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Preface

This Volume is part of the 'Case Studies in Innovation', as formulated by the OECD (DSTI/STP/TIP(2002)1). It is, however, a delimited and optional sub-study supplementary to the main case study on biopharmaceuticals.[1]

'Case Studies in Innovation' is ambitiously designed with the aim at answering one main research question: Can we identify important differences and similarities in the structure and dynamics of national biotech innovation system which explains the performance of this system? Then, what are the policy implications of this?

Since the sub-study has been conducted on a smaller and non-comparative scale as compared to the main study on biopharmaceuticals, it will not attempt to answer the overall research questions in full. We will, however, aim at presenting an overview of policy aims for this area as well as the current status of marine biotechnology in Norway, and on this basis tentatively sum up some policy implications.

The report has in overall been written and edited by Terje Grønning, with significant contributions in the form of authorship, co-authorship or input of individual sections by the research team members as follows: Eva Dobos and Dorothy Sutherland Olsen have contributed to Chapter 2, section 3.1 and Appendix 2. Mark S. Knell has written section 1.3 and supplied data for Table 3-9. Sub-sections 3.2.4 and 3.2.5 are based on the M.A.-theses of Ingeborg Frogner Dahl-Hilstad and Ovar Andreas Johansson respectively (Dahl-Hilstad 2003; Johansson forthcoming). The cover photography (courtesy of Anders Dahl-Hilstad) shows fish vaccination at Urke hatchery, Sunnmøre, Norway, in 2003.

We would like to extend our sincere thanks to interview and survey respondents, as well as to the members of the project's reference group (Grethe Foss, Henrik Lund, Torben Hviid Nielsen, Thor Amlie, and Tronn Hansen) for valuable comments and suggestions.

Oslo, 20 May 2004. Terje Grønning.

[1] The total amount spent on this part is approximately three man-months.

1. Introduction

1.1. Goals.

This Vol. II of the report on selected parts of the biotech innovation system in Norway describes and analyses the marine biotechnology sector. The report describes in particular initiatives for the development of drugs and processed biochemical resources, as well as the main traits of the economically significant aquaculture sector (mainly fish farming) as such and aquaculture supply functions related to biotechnology such as the development of fish feed and fish vaccines. Norwegian aquaculture does as a sector transcends borders by way of its ownership structure (Norwegian ownership in foreign fish farming firms, and foreign ownership in Norwegian firms, as well as foreign ownership of "Norwegian" fish health and fish feed firms). This overview does, however, serve as a guide to the public and business activities which are indeed concentrated to within Norway. There is also a brief description of the public R&D system which is of relevance. The aim is to present an overall outline of the current and potential barriers and drivers in the innovation chain, and on this basis arrive at relevant policy implications.

1.2. Approach.

1.2.1. What is marine biotechnology?

We use as the point of departure the OECD definition of biotechnology: "The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services". A firm or research institute conducting biotechnology research would adopt at least one of five technologies or processes:[2]

[2] Approved by the OECD Working party on Biotechnology in 2001 as the provisional statistical definition.

1) DNA (the coding): genomics, pharmaco-genetics, gene probes, DNA sequencing/synthesis/amplification, genetic engineering;

2) Proteins and molecules (the functional blocks): protein/peptide sequencing/synthesis, lipid/protein engineering, proteomics, hormones and growth factors, cell receptors/signalling/pheromones;

3) Cell and tissue culture and engineering: cell/tissue culture, tissue engineering, hybridisation, cellular fusion, vaccine/immune stimulants, embryo manipulation;

4) Process biotechnology: bioreactors, fermentation, bioprocessing, bioleaching, bio-pulping, bio-bleaching, bio-desulphurisation, bioremediation and biofiltration; and

5) Sub-cellular organisms: gene therapy, viral vectors.

We find it useful to follow up on this overall definition, and elaborate on its practical applications within the marine sector. One way of following up is to divide into five different research and business sub-areas, as follows:

a) Developing novel drugs;
b) Producing diagnostic devices for monitoring health;
c) Discovering new types of composite materials, biopolymers and enzymes for industrial use;
d) ensuring safety of aquaculture and fisheries;
e) Providing new techniques for management of marine environments; (ESF 2001: 6, with order altered).

Products already available have been derived from sponges, fish, and other organisms (Table 1-1). An interesting, although somewhat dated, overview assesses the commercial value of the various sub-areas (Table 1-2). Notable is the size of pharmaceutical and personal care applications with market value of 330 and 64 billion USD respectively in 1999.

The first sub-area in the list above, the sub-area related to drug discovery and development, has undoubtedly been the area attracting largest amount of attention in recent years (see e.g. Rayl 1999; Capon 2001; Spinney 2003; Haefner 2003; Tulp & Bohlin 2004). Indeed, it is acknowledged that the possibilities are still to a large extent unknown, since basic research in

Table 1-1: Examples of products from marine organisms

Products	Specific product	Source	Uses	Enterprise / trade Name
Algal polysaccharides	Carrageenans Agars Alginates	Red algae	Cosmetics, thickener, pharmacy, mucoprotector, anti-coagulant, antiviral	Marine colloids USA Danisco Denmark SOBALG France
Glycosamino-glycans	Chondroitin sulfate	Fish	Cosmetics, tissue replacement, anticoagulant	CTTP (France)
Chitosan	B (1-4) N-acetyl glucosamine	Crustacean shells, fungi	Cosmetics, colloids Pharmacy, Microencapsulation	
Lipids disease, mental development	Long chain PUFA (AA, EPA, DHA)	Microalgae, seaweed, fish	Prevention of heart disease, mental development is premature children; antimoural; lipid metabolism	BIONAGROL 3000 AGE OMEGA 3 (Arkopharma) MAXEPA (Pierre Fabre Medicament)
Peptides	Hormones, cyclic peptides	Fish, hydrolysates	Antioxidant, immunostimulants, nutraceutical products	Promarine

Note: Excerpts from ESF (2001: 7)

this area is at early stages relative to biotechnology research on human and plant material. In the case of humans and in the case of some plant species there have been large scale research projects going through several phases where, firstly, technology platforms necessary for the research and the development of protein analyses and bioinformatics tools have been developed. Subsequently, with advanced or complete gene sequencing of the species in question (such as the human being and the mouse in the case of mammals), it is possible to move on further with still more concrete projects. Within marine biotechnology, the progression is far behind, with only a couple of species fully sequenced thus far (Nerland 2004a: 115).

Table 1-2: Markets for biochemical resources, USD billions (1999).

Product category	Global sales	Sales derived from biochemical resources	Market value of biological inputs	R&D expenditures
Pharmaceuticals	330	188	14	46
Phytomedicines	14	14	8	NA
Agrochemicals	30	NA	NA	1.8
Seeds	30	30	NA	1.5
Enzymes	12	1.8	0.02	0.25
Personal care	64	7.6	1.2	1.0
Flavours/fragrances	14	2.2	NA	1.0

Notes: All estimates of R&D expenditures except pharmaceuticals are based on R&D as percentage of sales for top companies multiplied by global sales. Pharmaceutical sales includes purifed natural products, derivatives, and synthetic analogs of natural products. Seed market value of biological inputs: Private seed companies generally rely on their own germplasm collections. In addition, genetic resources for plant breeding programs can still be obtained at little or no cost from national and international seed banks.
Source: Artuso (2002: 1357).

Table 1-3: Examples of commercialized medicines from marine organisms

Chemical name	Origin	Activity	Molecule type	Commecialisation year
Cephalosporins	Marine fungi	Antibiotic	β-lactam	1965
Cytarabine (Ara-C)	Sponge	Antitumoral (cytostatic)	Nucleoside	1972
Kainic acid	Red alga	Anthelmintic insecticide	Amino acid	Early 1900s
Spongoadenosine (Ara-A)	Sponge	Antiviral Herpes	Nucleoside	NA
Ziconotide	Mollusc	Analgesic	Peptide	1999

Source: Excerpts from ESF (2001: 7)

However, one basic assumption is that there is in overall a rather great potential based on the simple facts that, firstly, the marine organisms are so diverse and numerous that interesting material is likely to emerge based on this fact alone, and, secondly, the fact that "natural products released into water are rapidly diluted and, therefore, need to be highly potent to have any effect" (Haefner 2003: 536). There are examples of successful applications already on the market (Table 1-3), and a relatively recent overview of drug candidates indicates the possibility of more products appearing on the market in the near or intermediate future (Table 1-4).

Table 1-4: Marine natural products and derivatives in clinical development.

	Compound name	Source	Chemical class	Company	Disease area	Status
Compounds targeting ion channels	Ziconotide	Cone snail	Peptide	Neurex	Chronic pain	Phase III
	AM336	Cone snail	Peptide	AMRAD	Chronic pain	Phase I/II
	GTS21	Nemertine worm	Anabaseine-derivative	Taiho	Alzheimer's disease Schizophrenia	Phase I/II
Compounds targeting enzymes	LAF389	Sponge	Amino acid derivative	Novartis	Cancer	Phase I
	Bryostatin-1	Bryozoan	Polyketide	GPC Biotech	Cancer	Phase II
	OAS1000	Soft coral	Diterpene-pentoseglycoside	OsteoArthritis Sciences	Wound healing Inflam-mation	Phase I/II
Microtubule-interfering agents	Dolastatin-10	Sea slug	Peptide	NCI/Knoll	Cancer	Phase II
	ILX651	Sea slug	Peptide	Ilex Oncology	Cancer	Phase I
	Cemadotin	Sea slug	Peptide	Knoll	Cancer	Phase II
	Disco-dermolide	Sponge	Polyketide	Novartis	Cancer	Phase I
	HTI286	Sponge	Tripeptide	Wyeth	Cancer	Phase I
DNA-interactive agents	YondelisTM	Sea squirt	Isoquinolone	PharmaMar/Johnson and Johnson	Cancer	Phase II/III
Oxidative stress inducers	AplidinTM	Sea squirt	Cyclic depsipeptide	PharmaMar	Cancer	Phase II
Lysosomotropic compounds	Kahalalide F	Sea slug/alga	Cyclic depsipeptide	PharmaMar	Cancer	Phase I
Immuno-stimulatory agents	KRN7000	Sponge	α-galactosyl-ceramide	Kirin	Cancer	Phase I
Calcium-binding protein antagonists	Squalamine lactate	Shark	Aminosteroid	Genaera	Cancer	Phase II
Compounds with unknown mechanism of action	IPL512602	Sponge	Steroid Phase II	Inflazyme/ Aventis	Inflammation Asthma	Phase II

Source: Excerpts form Haefner (2003: 542)

The second sub-area, diagnostic devices for monitoring health, relates to the phenomenon where "bioluminescent proteins from marine organisms are … under study in order to produce gene probes that can be employed to detect human pathogens in food, or fish pathogens in aquaculture systems" (ESF 2001: 8), whereas the activity concerning the development of new types of composite materials refers to exploiting the biochemical diversity in e.g. seaweeds for developing a variety of products (e.g. nutraceutics, biopharmaceuticals/health care, dental health care, novel excipients/delivery systems, enzyme biotechnology, biosensors, bio-energy, and bioremediation) (ibid.: 13).

Marine biotechnology may be applied for enhancing safety of aquaculture and fisheries in the sense of improving aquaculture production by way of "species diversification, optimal feeds and feeding, health of cultured populations and resistance to diseases, as well as minimal environmental impact" (ESF 2001: 11). For example, it may be perceived health and economic advantages – as well as environmental challenges - associated with the development of recombinant vaccines and DNA vaccines for use within aquaculture (Nerland 2004b; see also Section 3.3.3 below). In addition, "genetically modified organisms (GMOs) with particularly useful features such as fast growth, resistance to pathogens or low-temperature tolerance can be made available for basic research proposals by recombinant technology" (ESF 2001: 13). Another, technology is in theory possible, transgenic species, although rarely used due to consumer concerns in a number of countries. The development of polyculture is used in some instances for overcoming environmental problems within, e. g., Asian aquaculture.[3]

Some of these techniques may be coupled to a persisting problem within otherwise successful aquaculture, the problem of currently under-utilized waste material. there is an increasing and urgent need for " the upgrading of fish species or fish remains (skins, viscera, heads etc.) or shellfish (e.g. wastes of squid viscera, oyster, mussel) or of undesirable molluscs (e.g. the slipper limpet)" (ESF 2001: 11). One estimate is that there at a global level is directly accessible marine biomass up to 100 million tonnes per year, equal to approximately 10% of the animal protein consumed by humans (ibid.: 11-12).

In innovation system terms, one might want to conceive of all the five sub-areas as constituting a single and large marine biotechnology innovation system (Table 1-5). This might be conceivable in the case of dense international collaboration or in the case of a large economy with a large amount of activities across several sub-areas. In general, however, we

[3] Polyculture is the "integrated system of culture of different species in which the waste of one species provides food for another, achieving water filtration, removal of organic matter and increased production" (ESF 2001: 11).

find it more useful to conceive of the sub-areas as separate sub-systems, which may or may not cross over to other sub-areas. In other words, a particular marine biotechnology innovation systems may be specializing more in e.g. the development of new drugs than other innovation systems, whereas other systems may be specializing more into diagnostics devices, new materials, or aquaculture and fisheries supplies and marine environment management techniques (as seems to be the current case of e.g. the Canadian system, and as we will se below, the Norwegian systems). Each type of specialisation seems to requisite a special type of public ~private interaction as well as special types of science base.

This analytical framework may to a certain extent resemble a "linear" way of thinking where there seems to be a strong division of labour between the public, basic research sector, and the private, applied research sector. Empirical studies will have to show how this relationship turns out to function in actual cases. One case in question is based on the extraction of plant based material, and the industry turned out to target a narrow range of commercially important species "using high throughput in vitro screens followed by in vivo models" (Brown 1996: 270), whereas the research institute in question followed a strategy of "tackling a wide range of target pest and model species, initially through low-throughput in vivo contact assays" (ibid.). One might perhaps expect in the case of the three upper-half activities in Table 1-5 some collaborations between research based SMEs developing promising possibilities on the one hand and pharmaceutical and other large firms "taking over" at a certain point, much as in other parts of the biopharmaceutical industry (see Vol I). thus, based on the assumptions above there will in certain cases certainly be a high possibility for the direct collaboration between publicly funded research institutes and big business. One reported case tells how an externally funded non-profit organization has a research programme on deep-sea sponges running for eight years before entering into an agreement for the licensing and development of one of its discoveries, the anti-tumour compound discodermolide (Fenwick 1998: 300; see one of the microtubule-interfering agents in Table 1-4).

Table 1-5: Science base and public ~private interaction and of marine biotechnology innovation (sub)system(s).

	public	private
• developing novel drugs • diagnostic devices for monitoring health • new types of composite materials, biopolymers and enzymes for industrial use	existence of science base focusing on a wide range of species and advanced results in certain areas	industry willing to target and develop narrow range of commercially promising species
• safety of aquaculture and fisheries • providing new techniques for management of marine environments	policy and financial allocations to public sector for development of relevant knowledge base	industry willing adopt and/or develop new methods by way of implementing, if necessary, biotechnology

In the analytical framework outlined here the assumption is thus that the relationship does not necessarily have to function invariably in a strict linear way, but rather to underline an assumption for what seems to be a basic prerequisite for the development of a viable marine biotechnology innovation system: the enormous and risky endeavour it is to explore the biotechnological knowledge base necessary for further commercial applications on the one hand, and the assumed unwillingness of private actors to enter into such wide and risky endeavours on the other. Also in the vertical sense, it is conceivable that there might be systems specializing in one sub-area whereas other systems try to develop symbiotic inter-relationships between two or more sub-areas (e.g. development of new types of composite materials, biopolymers and enzymes for industrial use coupled to the existence of waste biomass from aquaculture and fisheries).

1.2.2. Data.

The report contains four steps in order to describe the marine biotechnology sector in Norway: (1) descriptive analysis of the national marine biotechnology innovation system; (2) interviews with selected actors in the system; and (3) analysis of the design and implementation of biotechnology use and.[4] The descriptive analysis of the national marine

[4] This Vol II does thus not include bibliometric and patent analyses due to methodological difficulties of classification, nor does it include analysis of collaborative patterns due to small sample size of aquaculture related businesses in our survey.

biotechnology biotech innovation system relies on primary sources such as information from interviews and survey responses. Firms' annual reports, relevant White Papers and policy statements from ministries and regulatory bodies as well as Internet websites of the various enterprises were also used for further analysis.

Since this is an optional sub-study within the "Case Study on Biotech Innovation Systems" project, the budget has not allowed for an extensive survey and comprehensive interviewing as in the case of Vol. I of the report. Within our Biotechnology Use and Development Survey there were 8 upstream aquaculture-related firms included within the respondents This number is obviously too small to serve as a basis for quantitative analysis. The responses are used as additional background material on an anonymized basis.[5] Interviews were conducted with selected firms and authorities:

- Firm specialising in genetics (1),
- feed producers (2 firms),
- vaccine producers (3 firms),
- authority for animal and health issues (1).[6]

As for secondary sources, e.g. Fraas et al., (2003) and IntraFish (various issues) have proved particularly useful within this context, since these sources describe the marine resource innovation system with an emphasis on the producers and sales part of the chain, areas which we have not had the resources to collect detailed information from. In addition, Sundnes & Sarpebakken (2003) provide detailed information on the input factor when it comes to R&D resources within the marine aquaculture sector at large.

The report is organized as follows. Due to the smaller scale of the research conducted for this report we have decided to structure it in a more compact fashion as compared to Vol. I. The remainders of this Chapter 1 is a brief description of country characteristics and identification of aquaculture's position within the economy at large. A description and

[5] The numerical results are included in the overall presentation in Vol. 1. To complement this survey, we cite from the *Statistics Norway* aggregated 2001 *R&D and Innovation survey* to provide complementary data on fish farming firms.

6 Additional relevant interviews for the Vol II analysis conducted in connection with Vol. I's analysis included ministries (6), regulatory body (1), patent office (1), venture capital firms (2), Research Council of Norway (1), Regional Development Fund (1), Norwegian Trade Council (1). For a full list of the interviews conducted in the project, see Vol I.

analysis of R&D&T policies follows in Chapter 2, whereas in Chapter 3 we give an overview of the national public R&D system and the business system respectively. Chapter 3 also contains more in-depth descriptions of fish farming, fish feed development and fish health respectively when it comes to aquaculture activities, as well as a description of other marine technology businesses in Norway (e.g. biopharmaceuticals based on marine sources). Chapter 4 gives a synthesis and conclusions related to policy implications.

1.3. National economic characteristics and the marine sector

Norway is a small country with a population of slightly more than 4.5 million people.[7] Civilian employment was 2.3 million, with about 3.8 per cent employed in agriculture, forestry and fishing, 21.5 per cent in industry and construction and the balance in services. In 2001, the OECD estimated its Gross Domestic Product (GDP) at €194 billion ($178.4 billion) in 1995 US dollars and exchange rates, or about €43 000 ($40,000) per capita. Gross fixed capital formation was about 19 per cent of GDP, and general government current revenue was over 57 per cent, the highest among OECD Member States. However, there was also a general government surplus of 14 per cent of GDP because of oil revenues in that year. The Norwegian economy relies heavily on natural resources, including oil, gas, hydropower and fishing. In 2001, oil and gas exports topped €86.6 billion ($77.6) and government oil revenues from these exports exceeded 15 per cent of GDP, which created large surpluses in both the government budget and trade balances. Little more than 63 per cent of the revenue obtained through exports was returned through the imports of goods and services in that year. An important consequence of these oil revenues is that the business cycle often moves in a different pattern from the rest of Europe.

Norway created this competitive advantage in natural resources over time. Geography played an important role, encouraging the development of the fishing, wood, iron ore and shipping industries for several centuries, and hydropower industry in the early 20th century. The discovery of oil and gas in the 1970s created dynamism over the past three decades that made Norway one of the wealthiest societies in the world, but also affected most other industries in the economy. Industries directly connected to the petroleum and gas industries

[7] This section is a summary of a more comprehensive account of the Norwegian economy by Mark S. Knell, section 1.3 in Vol. 1 of the report.

often developed a competitive advantage, while other industries were often faced by rising wage costs and exchange rate. The OECD (2002, p. 23) observed that competitiveness had deteriorated by 24 per cent between 1995 and 2001 in terms of unit labour costs and by 7 in terms of wages per hour in manufacturing.[8] While there has been considerable productivity growth over the period, captured in the difference between the two measures of competitiveness, the information and communications (ITC) sector and biotechnology-related industries remain small relative to its Nordic neighbours. This is partly because of technological trajectory followed by Norway.

Table 1-6: Structure of Production in Norwegian Manufacturing, 1990 and 2000

		Total output		Value Added		Employment		Exports	
		share	change in share	share	change in share	share	change in share	share	change in share
		1990	2000	1990	2000	1990	2000	1990	1999
Food, beverages & tobacco	15-16	23.4	–1.3	15.1	1.4	17.4	0.7	9.2	2.4
Textile & leather products	17-19	1.7	–0.4	2.2	–0.6	3.5	–0.8	1.4	–0.3
Wood & cork products	20	4.8	–1.0	5.2	–1.2	6.7	–1.4	1.9	–0.5
Pulp, paper, printing & pub.	21-22	13.5	–2.0	16.9	–1.8	16.4	–0.5	8.3	–1.5
Coke & petroleum products	23	6.0	–6.0	1.7	–1.6	0.6	–0.6	9.9	4.2
Chemicals ex. pharmaceuticals	24ex2423	6.9	–6.9	7.4	–7.3	4.6	–4.6	12.3	0.3
Pharmaceuticals	2423	0.9	0.9	1.4	0.6	0.8	0.4	1.5	0.8
Rubber & plastic products	25	1.9	–0.3	2.5	–0.5	2.2	–0.2	1.7	–0.4
Other non-metallic prod.	26	2.9	–0.1	3.9	–0.3	3.5	–0.4	1.1	–0.4
Basic metals	27	9.7	0.3	8	1.2	5.8	–0.8	20.8	–3.3
Fabricated metal prod.	28	4.0	0.2	5.6	0.4	6	0.3	2.7	–0.4
Machinery & equip.	29	6.0	0.4	7.9	–0.2	7.9	0.5	7.3	0.2
Office & computing mach.	30	0.8	–0.5	0.9	–0.8	1	–0.8	1.9	0.1
Electrical machinery	31	3.2	–0.7	3.7	–0.7	3.8	–0.6	2.2	0.7
Radio, tele. & comm. equip.	32	1.1	1.2	1.5	1.4	1.6	0.7	1.6	1.2
Medical & precision inst.	33	1.0	1.0	1.4	1.0	1.3	1.3	1.5	0.7
Motor Vehicles & Trailers	34	1.0	0.4	1.1	0.5	1.1	0.6	2.2	0.3
Building & repairing of ships	351	7.5	1.7	8.3	1.6	9.2	2.2	9.7	–4.8
Aircraft & apacecraft	353	0.8	–0.6	1.5	–1.1	1.4	–1.0	1.3	–0.4
Railroad & other transport	352+359	0.6	–0.4	0.8	–0.6	0.9	–0.6	0.1	0.0
Other manufacturing; recycling	36-37	2.4	0.8	3.2	1.0	4.1	1.2	1.3	0.7

Source: OECD Stan database, 2003.

Since Norway relies heavily on natural resources, it devotes a relatively low percentage of GDP to manufacturing. Without the petroleum sector, Norway's GDP would be much lower

[8] The relative trade-weighted unit labour costs also increased by 32 per cent during this period, but the OECD found that all but 2 per cent of this rise was offset by a decline in profit margins (OECD 2002). The European Commission (2002) maintains that competition deteriorated by 15 per cent vis-à-vis other industrial countries.

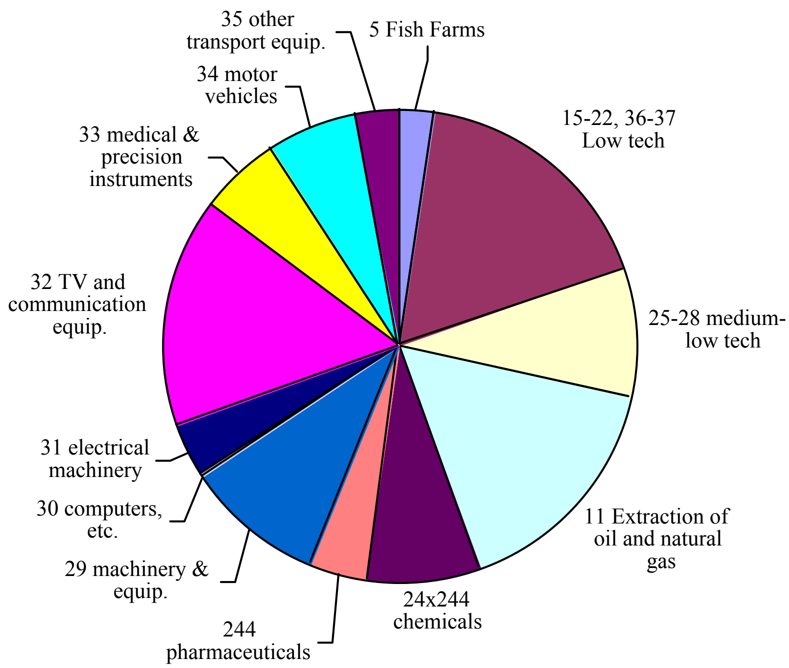
and the share of manufacturing would be higher. Declining competitiveness may have also influenced the growth of manufacturing over the past two decades. Manufacturing value added increased by an annual average of over one per cent from 1994 to 2001, but this followed twenty years of stagnation. Table 1-6 shows the industrial structure in 1990 and the change that took place during the decade. Food and beverages, pulp and paper, chemicals (including pharmaceuticals) and ship-building were the four main industries during the decade, with pulp and paper and chemicals losing the greatest share and ship building making the largest gains. Machinery and equipment remained rather constant because it is an important supplier to the petroleum sector. Pharmaceuticals made up less than one per cent of manufacturing output in 1990, but gained almost one percentage point during the decade.

The extraction of energy producing materials and other mining output made up 57 per cent of Norwegian exports in 2001. Of the remaining commodities, foodstuffs (including fish and fish products), paper and wood-related products and metals were important (see Table 1-6). We can note an increase in both share of export and in value added in the category Food etc. which includes seafood products. Although the manufacturing sector did not lose export market share in 2001, its share in GDP declined since 1995, with manufacturing exports lagging market growth by almost 2 percentage points per year. Manufacturing exports were concentrated mainly in the low and medium-low technologies. The reason may be that the competitiveness of tradeable goods deteriorated considerably from 1995 to 2001. However, the balance of trade in services was positive in recent years, mainly because of a large positive balance in sea transport, but the relatively large percentage of exports in business services indicates that Norway is developing a competitive advantage in certain high technology services.

The composition of business expenditures devoted to innovation, including research and development (R&D) activity emphasise the importance of the petroleum and natural gas sector. As Figure 1-1 shows, the high tech sectors (NACE 244, 30, 32, 33) make up less than one-third of R&D activity in industry. When the petroleum and gas sector is excluded, the share rises to 38 per cent, which is well below the other Nordic countries and the United States. Pharmaceuticals make up about 4 per cent of the innovation expenditures in industry, and about 2.5 per cent of total innovation expenditures by business enterprises. Innovation expenditures in various services make up about 40 per cent of total expenditures. The OECD

(2003) points out that almost half of total R&D activities performed by business are carried out in the service sector.

Figure 1-1 Innovation expenditure by industry in Norway, 2001



Source: Statistics Norway, Community Innovation Survey, 2001

The development of the Norwegian economy and the competitive advantage of some industries helps to explain the evolution of R&D activity during the past decade. It also helps to explain why R&D activity as a percentage of GDP is significantly lower than the OECD average despite a policy target to reach this average by 2005 (OECD 2002). One reason for the relatively lower R&D activity is that the industrial structure in Norway has a relatively lower share of R&D intensive industries, such as the defence, electronics and pharmaceuticals industries. If the defence-related industries are excluded from GERD, Norway compares more favourably to this average and is close to the EU average.

Nevertheless, Norway compares very favourably with the OECD average when R&D activity is measured as the number of researchers as a percentage of the workforce. Norway has about 1.5 more researchers per thousand workforce more than the OECD average, and the trend shows that the number of researchers should remain high. Some of the difference between R&D expenditures and R&D personnel may be due to the high priority given to the social sciences and humanities, where the link between research and productivity is typically weaker than in areas such as science and engineering. This may also explain why the average number of triadic patents granted per Norwegian researcher was only 5.4 patents per thousand workforce from 1993 to 1998, whereas it was 12.7 patents per thousand workforce in the OECD.[9]

Table 1-7: Gross Domestic Expenditure on R&D and Researchers, 2001

		Percentage of GERD financed by:		Percentage of GERD performed by:			Total Researchers
	million current PPP$	Industry	Govern-ment	Industry	Govern-ment	Higher Education	Full time equivalent
Norway	2,663.1	51.6	39.8	59.7	25.7	14.6	19,752
Denmark	3,204.1	59.0	31.2	64.9	19.4	14.5	18,944
Finland	4,676.8	70.8	25.5	71.1	18.1	10.2	36,889
Sweden	9,894.0	71.9	21.0	77.6	19.4	2.8	45,995
Total OECD	645,409.6	63.6	28.9	69.6	17.3	10.4	368,087

Source: OECD, Main Science and Technology Indicators, Volume 2003/1, p. 14.

As Table 1-7 shows, the government is a much more important source of finance for R&D activities than is typical in the OECD or even in the Nordic countries. The table also shows that the business enterprises also performs a much lower percentage of R&D activity than the OECD average and higher education and public research institutes perform a much higher percentage. Moreover, industry depended on foreign sources for more than 14 per cent of its business expenditures on R&D activity in 1999, which very high when compared with other countries in Scandinavia (OECD 2003). Foreign capital was crucial to the development of a lot of the resource-intensive industries in Norway.

[9] Triadic patents include patenting activity in the European Patent Office (EPO), United States Patent and Trademark Office (USPTO), and the Japan Patent Office

2. Overview on R&D&T&I policies

2.1. Main actors involved in policy making and policy programme management

2.1.1. General historical background

In fish farming, two principles have been governing policy: Equality, meaning an equal distribution of income; and preservation, referring to preservation of traditional settlements in the districts in Norway. In the 1970s, it was not desirable that the fish farming industry should turn into an intensive production, and the policy favoured a labour intensive mode of production as this should be an additional business for farmers and fishermen in the rural areas (Dietrichs 1995:6). However, during the 1980s it became clear that the Norwegian aquaculture industry was not living up to its potential, and it was hard to attract capital to an industry ravaged by diseases. The restriction imposed on it by the authorities to keep it labour intensive scared many potential investors and made them move the capital to other countries where the regulation was less restrictive. Considering the lack of capital and the potential in aquaculture, the government decided to turn the Norwegian aquaculture industry competitive (ibid.: 7).

The commercial breeding of salmon, established in the 1970s, was a radical innovation in the sense of developing a new fish farming industry. At the time of the first success the division of responsibility between institutions and governmental organisations was not clearly defined, and several disagreements occurred. These disagreements involved ministries in the sense that there were discussions about institutional control between the Ministry of Agriculture, Ministry of Fisheries, Ministry of Trade and Ministry of Environment. The discussions did not arrive at a satisfactory solution, and the regulation system for fish farming is still fragmented between several actors. The Ministry of Fishery considers breeding as fishery, the Ministry of Agriculture looks upon bred fish as a household animal, the Ministry of Industry considers fish breeding as a process industry, and Ministry of Environment views it as a an environmental challenge (Fraas et al. 2002: 67). The four ministries have different views on breeding, how breeding should be regulated and who should have the key responsibility for the whole sector. The fragmentation has an immense impact also on knowledge infrastructure and financial resources for research.

2.1.2. Actors

Several institutions at different levels provide public funding for R&D activity. Apart from the Ministries, the two key organisations at state-level are as reviewed also in Vol. I the Research Council of Norway (RCN) and the Norwegian Industrial and Regional Development Fund (SND).

The Research Council of Norway (RCN) is the most important actor in shaping research policy in Norway. Run under the auspices of the Ministry of Education and Research, the RCN acts as a main research policy advisor and allocates research grants on the basis of guidelines drawn up by the Norwegian government. Approximately one third of Norway's public sector research investment is channelled through RCN. The remaining is transferred directly from the ministries to the relevant research institutions. In 1999, the total expenditure on R&D was €2.4 billion (NOK 20.3 billion), of which public sector allocations accounted for roughly €1.02 billion (NOK 8.5 billion). In 2002 the Research Council of Norway had a budget of €0.47 billion (NOK 3.6 billion). The RCN not only manages these funds but also advises the government on research policy and has a strategic responsibility for the research institutes. Its 3 main functions are:

- Government adviser, identifying present and future needs for knowledge and research.
- Funding agency for independent research programmes and projects, strategic programmes at research institutes, and Norwegian participation in international research programmes.
- Co-ordinator, initiating networks and promoting co-operation between R&D institutions, ministries, business and industry, public agencies and enterprises, other sources of funding, and users of research.

Most RCN-funds are distributed through competitive means, using peer review of applications. Funding is allocated to research programs, independent projects, infrastructure, grants and fellowships. RCN negotiates its budget annually with each of funding ministries, which generally allocate funds for designated purposes. The Ministry of Trade and Industry is the largest contributor.

Norwegian Industrial and Regional Development Fund (SND) (now integrated into Innovation Norway, see below) had as its main objective the promotion of economically profitable business development and offered company financing, venture capital investment and financing of regional development projects. A public enterprise since its formation on 1 January 1993, it has been the government's primary instrument for promoting enterprise development throughout Norway. As an instrument for national and regional economic policy, the SND offered expertise and funding to companies in their early stages of development and promoted new and innovative business development by finding, refining, funding and following up interesting projects and enterprises. This also entailed developing and carrying out regional and national projects and programmes, financing viable small and medium-sized companies, and improving female participation in industry, among other things.

SND was established as a decentralised organisation with regional offices. The 17 regional offices, one in each county, and the head office situated in Oslo jointly possess both broad and more specialised in-depth competence. The head office constitutes a national competence and resource centre for business and regional development. It also carries the responsibility for management and control, as well as the follow-up of operations and results for the entire SND system. The regional offices are local resource centres for Norwegian trade and industry, and the majority of all applications are handled and decided here. The regional offices constitute the customers' main entrance to both SND and its partners, and form the gateway to all public financial instruments.

In 2001 SND were responsible for redistributing the sum of €0.57 billion (NOK 4.6 billion) for R&D purposes in more than 9.000 projects. This also included funding for the agricultural and fishery sector. 67 per cent of this amount was allocated to innovative projects and to newly established enterprises and existing companies. Although the amount allocated to innovation within the national venture capital scheme and development grants as a whole does not show any fundamental change, the share of innovation linked to actual new establishments is increasing. While there is no public data on the proportion of SND funds allocated to biotechnology, it is estimated that €3–4 million (NOK 20-30 million) was allocated in 2002, while the total amount allocated to innovation projects was €74.9 million (NOK 600 million) (interview, June 2003). Within fish farming 5 projects were funded in 2002. 3 were in the form of grants, and 2 received loans (interview, May 2004).

Innovation Norway: On 1 January 2004 Norwegian Industrial and Regional Development Fund (SND) merged with the Norwegian Tourist Board and the Government Consultative Office for Inventors, SVO to create a new public organisation, 'Innovation Norway' (Norwegian Ministry of commerce and trade, 2003). The main objectives of the organisation are similar to those of the SND, especially in the promotion of innovation and internationalisation of small and medium enterprises as well as promoting regional development.

Other related policy actors in biotechnology innovation are organisations and institutions that contribute to shaping the government's policy by playing advisory role in various issues. Such organisations are non-governmental organisations (e.g. Norwegian Biotechnology Association), governmental organisations (e.g. Biotechnology Advisory Board, Ethic Committees), and initiatives for international cooperation (The Trade Council of Norway, which merged into 'Innovation Norway' on 1 January, 2004). Business is represented by several organizations, including the Fish Exporters' Association.

2.1.3. Public funding of marine biotechnology.

The main funding organisations of marine biotechnology research in Norway are the Ministry of Fisheries, the Ministry of Education and Research, the Ministry of Environment and the Ministry of Trade and Industry. The funding is channelled through The RCN and several institutes and universities. In addition, the former Norwegian Industrial and Regional Development Fund played a role in funding of biotech project as co-funder, mostly for applied research and development projects.

Table 2-1: R&D expenditure within aquaculture according to sector and main financing source (2001; mill € and percent)

Financing	University sector	Institute sector	Business	Total	Percent
Public	13,4	25.9	1.4	40.7	53
Private	0.72	6.8	23.9	31.4	41
Other sources	0.69	0.5	…	1.2	2
Foreign	0.88	2.2	…	3.1	4
Total	15.7	35.4	25.4	76.4	100

Note: Business sector's R&D ration was at the time of publication of the cited report a preliminary estimate.
Source: Sundnes & Sarpebakken (2003: 9).

The research carried out at the Norwegian research institutes (see Chapter 3) is on the one hand heavily concentrated on salmon, with a total expenditure of €47.8 million (NOK 384.7 mill.) within this area alone in 2001, while at the same time as there is an increasing expenditure on other marine species (Table 2-2). In looking at the different categories, it is interesting to note that the biotechnology related areas "Health and diseases", "Feed, feed resources and nutrition" and "Breeding and genetics" rank among the top four research areas in terms of funding allocation (Table 2-3 and 2-4).

Table 2-2: R&D expenditure within aquaculture 1998-2001 according to salmon species and marine species (mill € fluctuating prices)

Area	1998	2001
Salmon species	28.4	47.8
Marine species	13.7	24.3
Total	42.1	72.1

Note: Excluding large scale investments.
Source: Sundnes & Sarpebakken (2003: 13).

Table 2-3: R&D expenditure within aquaculture 1995 & 2001 according to Research Council programme category (percent)

Category	**1995**	**2001**
Health and diseases	25	18
Production and management: Larvaes etc.	10	16
Feed, feed resources and nutrition	24	20
Breeding and genetics	2	11
Technology and equipment	4	11
Slaughtering, distribution, quality and measurement	4	7
Production and "drift": Fish for food	8	6
Environmental effects studies	3	3
Economy, markets and society	2	3
Others	11	3
Cultivation related measures	7	2
Total	100	100

Note: "Cultivation related measures" implies relationship between fish farming and natural fisheries, etc.
Source: Sundnes & Sarpebakken (2003: 14).

Table 2-4: R&D expenditure within aquaculture 2001 according to Research Council programme category and area (mill € & percent)

Category	Salmon species	Marine species	Total	Percent
Feed, feed resources and nutrition	10.8	3.6	14.4	20
Health and diseases	9.3	3.9	13.2	18
Production and management: Larvaes etc.	3.9	7.4	11.2	16
Breeding and genetics	5.5	2.4	7.9	11
Technology and equipment	6.2	1.9	8.1	11
Slaughtering, distribution, quality and measurement	3.7	1.4	5.1	7
Production and management: Fish for food	2.9	1.4	4.3	6
Environmental effects studies	1.7	0.8	2.4	3
Economy, markets and society	0.8	1.2	2.0	3
Others	1.7	0.2	1.9	3
Cultivation related measures	1.2	0.2	1.4	2
Total	47.8	24.3	72.1	100

Note: Excluding large scale investments. "Cultivation related measures" implies relationship between fish farming and natural fisheries, etc.
Source: Sundnes & Sarpebakken (2003: 19).

2.2. Main regulations, policies and research programmes

In this section we describe general regulations and policy initiatives and subsequently review recent and current policy instruments (i.e. research programmes) relevant to aquaculture. Although Norway was the first country in the world to establish an independent Ministry of Fisheries, the policies affecting aquaculture originate in several different government ministries. Those involved are the Ministry of Fisheries, the Ministry of Agriculture, the Ministry of Trade and Industry and the Ministry of Environment.

2.2.1. Main regulations and policies

As mentioned in Vol. I of this report the Norwegian government recognised the need to support certain “strategic” technologies. In the period from 1978 to 1991, Norway implemented a technology policy targeting research in certain technologies where it either had a natural advantage, or was already a competitive (Norwegian Government White Paper no. 54:1982-83). The Ministry of Trade and Industry targeted five technologies: IT, biotechnology, material technology, aquaculture and off-shore technology. A government white paper (no. 48:1994 – 1995) states that marine resources should be the driving force Norwegian coastal industry.

Policies.

A National strategy for business-directed biotechnology (Ministry of Trade and Industry, 1998) outlines overall goals and areas for emphasis in the future. The overall goals are to improve the competitiveness of Norwegian industry by way of concentrating R&D to those areas where Norway has good opportunities to succeed internationally. The policy-makers are of the opinion that there is great potential for value added biotechnology based production, albeit with the necessity of concentrating further efforts to selected areas. These four areas are medicines and health, food production, and marine biotechnology. As for marine biotechnology, the potential lies in the existence of a rich marine biodiversity combined with a certain natural science research tradition within the field. However, the commercialisation of this potential is yet to be seen in earnest. Thus the plan advises a continuation of existing processes combined with creation of new industrial processes.

Examples given for potential future efforts are fish farming, aquaculture, management of resources, exploitation of marine molecules, and environment.

The Fisheries and aquaculture: R&D strategy plan 1999-2003 (Ministry of Fisheries 1999) also divides activities into four areas. The first three areas being especially relevant to the topics in this study.[10] Firstly, "Resource- and environment-related research and surveillance" is to secure an optimal knowledge base for the sustainable exploitation of Norway's marine resources. Within this area there is international collaboration with The International Council for Exploration of the Sea (ICES). Secondly, "Aquaculture research" is aimed at opening new avenues of business as well as securing sustainability. A particular area emphasised is the maintenance of competence within fish farming. "Market and business-directed research" is geared towards increased competitiveness and ability for restructuring.

Then, in the same year the Norwegian government white paper on Research entitled "Research at a Watershed" (Norwegian Government White Paper nr 39:1998 – 1999), four areas are identified for special attention: marine research, information and communication technologies, medicine and health, the crossroads between environment and energy. In this White Paper marine research is designated to be embedded in a value chain perspective, where one sees the whole production process as a whole: from fisheries and fish farming on the one side to marketing and sales on the other. The sector's understanding of consumer behaviour, consumer patterns and trade policies is to be improved. New processing methods are to be developed in order to secure a high quality of the products. Moreover, marine biotechnology research aimed at understanding how marine resources may be utilized in food products, pharmaceuticals and cosmetics is to be strengthened.

We have not reported the amount and character of activity before or after this period (1998-1999), but based on our survey of relevant documents we find that there was an increased and formulated interest in this area around this time. Incidentally, an academic group also proposed policy measures at exactly this timing (Almås et al. 1999), urging for the increased attention on utilization of marine resources. This group did under the auspices of the Royal Norwegian Science society prepare a recommendation for increased research efforts, where

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[10] The fourth area is "R&D related to harbours and infrastructure for ocean transport".

the development of new species for farming figures in a central position. Biotechnology figures explicitly as one of the areas of attention:

> "Within a [future] framework programme for sea ranching research aiming at the development of chemical and biotechnological methods for toxin control of seafood should receive substantial support (…) The development within modern biotechnology has opened up for new approaches for improvement by way of breeding when it comes to marine algaes. It is just a matter of time and money when whether we want to know the complete genome of important seaweed species. This will give us opportunity to alter the chemical composition of the plants in the desired direction" (ibid.: 27).

The aim for this type of research would be two-fold: on the one hand it would be beneficial for the development of new feed types for use within aquacultuire. On the other hand, it would enable production of energy carriers or industrial chemicals (ibid.).

Legislation.

Although the above polices and guidelines are aimed at increasing research and improving opportunities for commercialisation of aquaculture, there is also legislation which may to a certain extent function as a barrier to this development. The Act on Gene Technology, came into force in 1993 (updated June 2001) It regulates the manufacturing and use of GMOs, the contained use and deliberate release and marketing of GMOs including micro- organisms, plants and animals used in research and industry production. Regulation on DNA vaccines is presently being debated by policy making bodies. So far, no DNA vaccines are produced or marketed in Norway. Genetic modification of fish is regulated by the same Act. The Norwegian law is in accordance with EU directives on contained use and on deliberate release of GMOs, but is, however, currently one of the most restrictive in Europe. Although the act is not particularly restrictive to aquatic GMOs, it could be a potential barrier for marine aquaculture. So far the more cautious attitude evident in the Norwegian act has not yet been put to the test with regard to the aquaculture industry, this is mainly due to the current public scepticism to GMOs in the major markets.

The following other Acts regulate aquaculture:

- The Act relating to sea ranching ("Lov om oppdrett av fisk, skalldyr m.v." 21 June 1985, and updated in 2003) regulates all activities related to breeding and rearing of fish in captivity for the purpose of consumption. This law includes restrictions on licensing of those permitted to run fish farming businesses (Crustacean and Echinoderm Sea Ranching Act ("Lov om Havbeite") passed in December 2000 and supplementary regulations published in 2003) and is similar to the act on fish farming, but regulates shellfish.
- Act relating to aquaculture ("Lov om tiltak mot sjukdom hos akvatiske organsimer" 22 June 1990, and updated in 2003) regulates health, hygiene and control of aquaculture establishments.
- Regulation on quality of fish and fish products ("Kvalitetsforskrift for fisk og fiskevarer") regulates production and transport of fish and all bi-products.

One of the key elements in the Act relating to sea ranching is the directive on licensing. This means that prospective fish farmers need an individual permission from the authorities. However, this rule does not differ from other fish producing countries` regulation. A recent study emphasises that the dialogue between the authorities and industry is good, and this has had a significant input when it comes to increasing market shares for Norwegian fish in the EU area (Fraas et al. 2002).

At present a working group on biodiversity ("Biomangfoldutvalget") is evaluating the need for legislation on biodiversity. This includes ownership and rights to exploit genetic material originating in the Norwegian coastal waters. The group will suggest new legislation based on Norway's commitment to the UN resolution on biodiversity (May 2000) and will deliver their suggestions in June 2004.

The existing legislation on marine resources is at present being revised to include specific issues around the development and exploitation of marine resources. It is also expected to give guidelines on marine R&D. Norway's commitment to regional development and the obvious importance of all marine resources in the development of coastal areas would suggest future policies being favourable to aquaculture, however both the results from the biodiversity group and the new law on marine resources may result in certain restrictions or challenges for the future development of aquaculture.

2.2.2. Research and commercialisation programmes.

A long-term governmental funded research project Healthy Fish (Frisk Fisk), running from 1983 to 1996, made a significant contribution to turning fish breeding in to a more attractive commercial activity. The project increased the knowledge base on fish diseases, which was the main problem in the breeding industry. New regulation was introduced and attention was turned also to areas such as planning and better hygiene in breeding plants. As a consequence, the industry was given a boost, and the public expenditure on R&D rose by ca 300% from 1984 to 1989. More recently, there has been a specialisation into various areas of relevance to biotechnology within aquaculture, as well as programmes aimed at commercialisation.

Research programmes.

FUGE (Functional genomics in Norway) represents, as described more in detail in Vol. I. section 2.2.1, a cooperative effort between Norwegian universities, research institutes and the industrial sector. The resources are to be allocated to basic biological research, health care research and marine research. The strategic plan for 2003-2004 indicates that the program aims to develop the fish industry, exploit the marine resources and in a long term, create a bio marine industry cluster in Norway. The goals for the two years in question are defined as:

- Integrate functional genomics into research related to bioprospecting
- Establish research groups which work on genetic conditions for growth, taste, reproduction and disease resistance for key fish species
- Improve the systems for feed production

In conjunction with this, there has been a established a Centre of Excellence at the Norwegian Agricultural University (NLH), with special focus on optimal use of proteins in fish feed and safety tasks in fish health.

BIOT 2000 (Biotechnology 2000) is a research programme within the research area formerly called Bioproduction and manufacturing. The programme does not concentrate exclusively on marine issues. A large number of the projects are however relevant. Some selected examples are:

- Development of molecular genetic methods for the identification and quantification of fish and seafood
- Sequence and function of immune genes in marine species
- Probiotics in scallops larviculture
- Effects of environmental stress on the development of the immune system, growth and survival in the early life stages of wild salmon

The examples show that the programme accommodates projects from basic research to more applied research, and that the topics range from production oriented topics towards topics related to environmental consequences of such production. The programme functions 1996-2005, and the total budget for this period and its 99 projects was approximately €19.9 (NOK 160 million), which means a simple average of approximately €0.20 mill. (NOK 1.6 million) per project (NFI 2003).[11]

Other research programmes that may be of direct or indirect relevance to academic or business partners are, mainly, Basic business directed biotechnology (acronym: GRUNNBIO), Biological diversity (BIOMANGFOLD) and Foodstuffs (MAT).[12]

Programmes for innovation and commercialisation.

The Norwegian government has also allocated considerable sums to programmes not directly related to research, but rather aimed at increasing R&D activities within private firms. Such programmes relavnt in this context include Enterprise development from medical research

[11] Amongst the projects were, though, also the funding of an information staff member and co-funding of a project called Ethics, society and biotechnology. The actual average for the natural science projects is, thus , higher.

[12] Still more, albeit more specialized, programmes are Process- and biomedical industry (PROSBIO; see description in vol. I), Pharmacology and pharmaceutical research (FARMA), Basic disease mechanisms (GRUSYK), and Molecular medicine and gene technology (GEN).

(MEDKAP), Mobilization for R&D-related innovation in small and medium sized enterprises (MOBI), and Commercialization of R&D-results (FORNY). A recent tax abatement programme (SKATTEFUNN, see Vol. I) gives, according to certain criteria, tax abatement for investments in R&D.

3. Structure and dynamics of the marine biotechnology system

3.1. National public R&D system

3.1.1. Overview

The Norwegian state provides considerably more than half of the funding for aquaculture R&D conducted in Norway (Table 3-1). But even a simplified overview of the national innovation system with regard to marine biotechnology shows a significant number of actors, both within the public and the business sectors (Table 3-2). Still, and as we will argue elsewhere in the report, the chart and description here is rather artificial in its domestic orientation, since the marine biotechnology transcends borders by way of its ownership structure (e.g. Norwegian ownership in foreign fish farming firms, and foreign ownership in Norwegian fish farming; foreign ownership of "Norwegian" fish health and fish feed firms). The simplified overview does, however, serve as a guide to the public and business activities which are indeed concentrated to within Norway.

Table 3-1: Total R&D-expenditure within aquaculture 1989-2001 according to main funding source, mill. NOK.

	1989	1992	1995	1998	2001
Public funding	282,3	280,4	203,4	194,1	327,7 (40.7 mill. €)
Private funding	126,0	85,4	145,9	183,1	287,6 (35.7 mill. €)
Total	408,3	365,8	349,3	377,2	615,3 (76.4 mill. €)

Note: For 2001 there is a break in the series due to a new type of mapping methodology.
Sources: Fiskeridirektoratets ernæringsinstituttet (1989-2001) and NIFU, as cited in Sundnes & Sarpebakken (2003: 12).

Table 3-2: Structure of the Norwegian marine biotechnology system, domestic part.

	Actor type	Role / examples
The national R&D system	Universities & colleges	Education and research: Veterinary University (NVH), Agricultural University (NLH), University of Bergen, Fish Academy at Tromsø University, University collage in Bodø, University collage in Ålesund,. Business School of Norway (Centre for fish economics), 7 marine-related colleges, 17 regional teaching units
	Governmental research institutes	Research: Matforsk (food research), Akvaforsk (aquatic research), Havforskningsinstituttet (marine research), fisheries and aquaculture research (mainly clusters in Tromsø and Bodø)
Business system	Firms in middle: Fish farming	Production and/or sales: 900 companies (150 export organisations)
	Firms downstream: Marketing/sales	
	Firms downstream: Processing (for food industry, from waste, for other industries)	Mostly moved out of the country due to labour costs
	Firms downstream: Transportation	Misc. firms
	Firms upstream: Fish health	Alpharma, Intervet Norbio, Scanvacc, VESO, Nutreco Aquaculture Research Centre (ARC), Inovio, Intrafish,
	Firms upstream: misc. research	AquaGen
	Firms upstream: Feed R&D, production & sale	Skretting (Nutreco), EWOS (Cermaq), EWOS Innovation AS, BioMar, Havsbrun Norge AS, Dana Feed Norge AS
	Firms upstream: Breeding, hatching, and smolt production	Approximately 1000 plants for salmon and trout breeding; 280 hatching, and smolt production plants
	Firms upstream: Production equipment	Misc. firms
	Firms not directly linked to aquaculture complex	Drug development, enzymes and materials
The environment	Public bodies for policies	Ministry of Fisheries; Ministry of Trade and Industry ; Ministry of Environment; SND; Research Council of Norway;
	Stimulation programs by the government	BIOT2000; FUGE; FORNY;Skattefunn.
	Regulation and regulation authorities	Act relating to aquaculture; Act relating to sea-farming; Regulations relating to fish farming and hatcheries; Regulation on quality of fish and fish products ; The Fishery Directorate
	Financing and insurance	Banks, Insurance firms
	Business support organisations	Biomarine Forum; Norwegian Seafood Export Council; 31 Fishing organisations; 14 Production, organisations; 12 Export organisations; 15 Other related organisations. Fiskeri- og Havbruksnæringens forskningsfond (FHF).

Source: field research.

3.1.2. Education and research institutes.

All four of the national universities, located in the cities of Oslo, Bergen, Trondheim and Tromsø, have programmes and conduct research in areas relevant to the development and maintenance of a biotechnology innovation system at large. Each of them specialize in particular fields related to biotechnology. The University of Bergen has the Broegelmann Research Laboratory, which specializes in immunology research and Sars International Centre for Marine Molecular Biology (est. 1997). The aim of the Sars Centre is to study basic biological processes in marine organisms using functional and comparative molecular methods on marine models. The research involves "studies of zebrafish, salmon genome, immune systems of fish and marine vertebrates" (UNIFOB 2003). The University of Tromsø has the Norwegian College of Fishery Science. Other universities also have courses within the relevant disciplines, as do regional colleges although predominantly not on the post-graduate level in the latter case. Two specialised universities that also conduct biotechnology research are the Norwegian University for Agricultural Studies and the Norwegian College for Veterinary Studies.

When it comes to education and research, the most striking feature is the high number of educational institutions both at University level and at University College ("Høyskole") level. The high number of institutions and teaching units may result in deterioration of the quality of education and research at Universities due to the spread of educational resources to many locations.

Location of public and semi-public research institutes.

Public and semi-public research centers are predominantly publicly funded, but do also negotiate for contracts with business as well as compete for academic funds. For the year 2001 the ratio of funding was 72 percent public funding, 20 percent business contracts, and 8 percent miscellaneous other sources, including foreign such as participation in EU projects (Sundnes & Sarpebakken 2003: 25). Appendix 1 gives an overview of both public and private research organisations.

Regarding the localisation of research actors , four key clusters can be noted. Firstly, the northern Norway cluster hub is Fisheries Research ("Fiskeriforskning", also called Norwegian institute for fisheries and aquaculture research, Inc.), and is a unit within the research consortium the NORUT Group. The consortium owns 51 percent and the Ministry of Fisheries owns 49 percent. The objective is to conduct research and development activities which is conducive to optimal use of marine resources. In addition the consortium acts as advisor to the authorities and business. There are ca. 100 employees in total.[13] The Norwegian College of Fishery Science (Norges fiskerihøgskole - NFH) is part of Tromsø University and has got national responsibility for building knowledge and competence within all areas of fisheries- and aquaculture research, as well as educate candidates for fisheries management and research, including an international degree "Master of Science in International Fisheries Management".

Mid-Norway research complex, i.e. mainly the city of Trondheim area, consists of a number of natural sciences departments including the Department for biotechnology at the Norwegian University for Science and Technology (NTNU), as well as relevant departments at the largest research foundation in Norway SINTEF (e.g. SINTEF Fisheries and Aquaculture, i.e. "SINTEF Fiskeri og Havbruk").

Western Norway, i.e. the Bergen area, consists of, firstly, the Institute for Oceanic Research ("Havforskningsinstituttet") which is a national research institute directed by the Ministry of Fisheries. The institute is the largest in Norway within the areas marine environment, marine resources, and aquaculture. The institute has ca. 500 employees. Institute for marine biology ("Institutt for fiskeri- og marinbiologi", IFM) at the University if Bergen educates and researches within the fields marine biology, fish biology, aquaculture and fish health. There are ca. 90 employees.

Eastern Norway research institutes, i.e. Ås and Oslo, consists of several research institutes and educational institutions, including VESO, the Norwegian school for Agriculture and the Norwegian School for Veterinary Studies. Amongst the research institutes is AKVAFORSK (aquatic research).

[13] Figures in this section are from Ministry of Fisheries (2003).

3.1.3. Recent developments.

The "Aqua Research Alliance" was recently formed as an autonomous, publicly funded collaboration, which attempts to link research activities across traditionally separate fields and includes the AKVAFORSK, The Norwegian Agricultural University and governmental research institutes in both nutritional and aquatic research. There are over 80 researchers participating in this collaboration. The prioritised research areas are nutrition and feed, genetics and breeding, product quality, optimisation of production, production of marine smolt, and production techniques and fish processing. The alliance also owns and manages the Centre for Integrative Genetics (Cigene), and the Aquaculture Protein Centre (APC) Many of the R&D projects organised by the alliance are in cooperation with industry, with both publicly and privately owned research institutes and universities in Norway and abroad. The collaboration also aims to contribute to education in this field.

To meet the increased demand for research in aquaculture, the Norwegian government allocated € 1.2 million (NOK 10 million) in 2003 to the creation of a marine research company called Protevs AS. This company is owned by the University of Bergen, Institute for Oceanic Research and the National Institute for Nutrition and Seafood Research, and offers contract research possibilities related to resource surveillance, fish farming, food safety, fish health, regulations, economics and marine biotechnology. The company will offer research services to Norwegian and international customers and will consolidate Norway's central position in marine research.

Another relevant actor is the independent foundation Rubin (www.rubin.no). This foundation aims raining awareness through relevant projects and reports, and thereby contribute to the increased total usage of the fish caught or raised,. Thereby an added value for the so called bi-products (waste like heads etc. resulting from the slaughtering process) can be secured.

3.2. Business system.

3.2.1. Overview.

We have, as reviewed in Chapter 1, suggested the following sub-divison of marine technology:

1. developing novel drugs;
2. producing diagnostic devices for monitoring health;
3. discovering new types of composite materials, biopolymers and enzymes for industrial use;
4. ensuring safety of aquaculture and fisheries;
5. providing new techniques for management of marine environments; (ESF 2001: 6, with order altered).

Sticking to this five-part way of structuring the description, business activities in Norway are according to our mapping exercise mostly concentrated within the first, third and fourth areas (Table 3-3).[14]

Table 3-3: Firms within marine technology, 2004 (indicative)

Category	Drug development		Materials, biopolymers and enzymes	Safety of aquaculture and fisheries/ new techniques for marine management		
Sub-category	Drugs for humans	Fish health		Genetics	Feed	Misc.
Firms	4	3	15	2	4	3

Note: For further details on firms, see Appendix 2.
Source: Field notes.

The fourth and fifth areas may in some cases overlap, and we have listed the two areas together in Table 3-3.

[14] We interpret the second area, as reviewed in Chapter 1, the actual use of marine materials within development of diagnostic processes, and have thus not found any activity in this area. Feed firms are in realty more numerous, but those not included are foreign and do only have sales activities in Norway. There are firms within breeding and hatchery which might have been included, since these sometimes conduct experimental activities related to the breeding of alternative species, but we have refrained from doing so due to lack of resources for doing a detailed study on this part.

The relationship between various current and potential future activities within the aquaculture may be divided roughly into activities in the middle (i.e. production of sellable products), upstream activities consisting of various inputs to the main part (R&D etc.), and downstream activities consisting of facilitating turnover of the production (transportation, sales). It is a distinctive trait of the aquaculture system at large that there is a fairly strong firm-level division of labour between the various activities. Although there exist integrated larger firms with activities ranging from production to sales, as well as to R&D, the more common case is that there is a concentration on a particular activity, i.e. the production firm selling the produce to a trading the company, or the production firm purchasing various upstream activities from external sources. Fraas et al (2002: 82) do in their study of fish farming in Norway term this phenomenon as follows:

> "[T]he most characteristic trait about the structure is that there is, in spite of the existence of large corporations within the sector, a specialization and fragmentation when it comes to activities and knowledge. The strong supply firms have developed through close cooperation with … knowledge milieux. … In addition, many fish farming businesses have not on their own been able to develop scientific … competence when it comes to the basis for their own activity" Fraas et al (2002: 82).

This trait of marked sub-division constitutes at the same time a challenge for the maintenance and development of the parts of the system with particular relevance to biotechnology (Table 3-4).

Table 3-4: Upstream, middle and downstream activities in aquaculture

	Upstream	Middle	Downstream
Mainly non-biotech focus	Hatching, smolt production Production equipment	Fish farming	Marketing/sales Processing (for food industry, from waste for other industry) Transportation
Current or potential bio-tech focus	Fish health Genetics Feed development Waste treatment	Potential integration of currently supplied functions into fish farming itself	(Marketing/sales)

The parts of the system with special and particular relevance to biotechnology are, thus fish health, genetics, and feed development. One relevant activity is marketing and sales, although obviously not included in the biotechnology activities as such. However, and as mentioned elsewhere, the marketing and sales of genetically modified products has not been relevant neither in Norwegian aquaculture nor elsewhere thus far.[15]

We will next first briefly review the activities which are not directly linked to aquaculture support functions (drug development and discovering new types of composite materials, biopolymers and enzymes for industrial use), before moving on to a description of the aquaculture support functions (fish health and genetics R&D).

3.2.2. Development of novel marine-based drugs

Pharmaceuticals-related research from marine resources are yet to be developed in an extensive scale. There are, however, some existing examples, such as products developed or in the process of being developed by Pronova Biocare AS, Biotec Pharmacon ASA, and Hepmarin AS.

Pronova Biocare's predecessor was founded in 1838 as a firm specializing in the refinement of fish oil products. Pronova Biocare currently develops two main categories of products:

1. Purified fish oils with a relatively low content of Omega-3. Processing is limited to the removal of impurities. Most of the purified fish oils contain about 35% Omega-3, and the ratios between the different Omega-3 fatty acids vary.

2. Omega-3 concentrates which range from 55% all the way up to 92%. These products have all gone through process steps in order to increase their Omega-3 content (Pronova Biocare 2004).

[15] For example, the Chinese prefer that red meat fish remains brightly red even after cooking (Hansen 2003). It would probably be a possibility to develop such a fish. Likewise, Americans prefer a certain consistency in the fish for the American market (interview).

Omega-3 fatty acids are nutrients that are necessary for normal growth and functioning. The human body can not synthesize Omega-3 fatty acids, and they must therefore be supplied through the diet.

Biotec Pharmacon ASA was established in 1990 by researchers from the University of Tromsø. The founders had discovered in 1987 that disease resistance of Atlantic salmon was significantly enhanced by a special beta-1,3/1,6-glucan preparation. Later they found that the preparation had the same effect on piglets and other livestock animals, and could subsequently mean a commercially significant improvement of growth performance and feed utilization.

This early research was sponsored by Phillips Petroleum Company as part of its biotechnology development program. Currently the firm aims at developing further the area of innate immunity and of the role of immune modulating beta-1,3/1,6-glucans, and develop pharmaceutical products for humans.

Within its current form, both Pronova Biocare and Biotec Pharmacon could classify within the next group to be described (development of composite materials, biopolymers and enzymes) since most of the present-day activities seem to belong here. We have, however, included them in this drug developing group since Pronova Biocare is in the process of obtaining approval of one of its products as a prescription drug (Bodd 2004), and Biotec Pharmacon products are already in use within pharmaceutical research (Biotec Pharmacon n.d.).

Hepmarin AS is a newly established firm aiming at developing anticoagulants based on marine products. The firm is spun off from the science park BioParken located in conjunction with the Norwegian Agricultural University.

3.2.3. New types of composite materials, biopolymers and enzymes for industrial use

We have indications, as shown in Table 3-2, that development of composite materials, biopolymers and enzymes may be the most heavily populated group when it comes to marine technology firms in Norway. The types of firms vary, however, from subsidiaries of multinationals to smaller, local firms. An example of the former is Firmenich Bjørge Biomarin AS. Originally a local firm (Bjørge Biomarin AS) established in 1988, it was acquired by the Swiss-based flavour multinational Firmenich in 2002. It continues to be managed by its founders and former owners. Products are natural seafood extracts, which subsequently contribute to the range natural ingredients available to Firmenich flavour scientists and technicians.

Another example is FMC Biopolymer AS (subsidiary of the multinational FMC Biopolymer). This firm produces biopolymers (alginates and carrageenans) processed from seaweeds and microcrystalline cellulose.

Biohenk, subsidiary of the multinational Cognis, produces chitosan from prawn shells and sells the products mainly to the cosmetic industry.

As examples of local (i.e. domestic) firms, Maritex AS is a subsidiary of the large dairy products firm Tine. Maritex conducts research on marine ingredients for use in dietary supplements and fish and animal feed. Napro Pharma AS develops products from fish oils and omega 3 concentrates for the nutricutical industry, as well as bulk marine and vegetable oils for pharmaceutical use. Likewise, ProBio Nutraceuticals AS produces customised food additives based on fish oils mainly for dietary supplements and nutraceuticals.

3.2.4. Safety of aquaculture and fisheries: fish health.

Fish farming.

The most important specimen in Norwegian fish industry is Atlantic salmon, representing a significant export product for the country. Shellfish farming is slightly increasing, especially farming of blue mussels and oyster, and there is experimental breeding of cod in captivity. Modern fish farming as we know it is basically the placement of large metal or mesh net cages in the ocean to breed fish. This technology was pioneered in Norway in the 1960s, and later expanded to countries like UK, Ireland, Canada, USA and Chile. Norway accounts for a substantial added value in the industry, because the major product is a “valuable” fish like salmon. Norway is the world’s largest exporter of Atlantic salmon. Table 3-7 shows the amount of Atlantic salmon produced in the key producer countries in 2000 and 2001. A slight decline of Norwegian production and an upswing in Great Britain, Chile and Canada can be observed. In the history of Norwegian salmon breeding there is only one period except 2000 / 2001 when the production has declined, namely 1991/1992. However, there is a significant caveat which should be added to the interpretation of these and subsequent figures within this chapter. Increasing parts of the Chilean industry (and, partly, in the other countries as well) is owned by firms which have their home base in Norway. Indeed, there are also other actors present within this sector, such as Dutch Nutreco, which owns firms both in Norway and Chile, as well as North American and British firms.

Table 3-7: The world's production of Atlantic salmon (tons)

Country	2000	2001
Norway	419 000	415 000
Chile	150 000	219 000
Great Britain	124 000	149 000
Canada	77 000	86 000
Others	86 000	106 000
In total	856 000	975 000

Source: Statistics Norway, Eksportutvalget for fisk. Kontali analyse.

As for Norwegian engagement abroad, the focus has been mostly on Chile. The estimates are that Norwegian-owned firms will produce 20 percent of the salmon in Chile during 2004, and that this ratio will increase to 50 percent in the near future (*Dagsavisen*, 28 February, 2004). In addition the activity includes equipment and feed supplies by Norwegian firms.

The motives for Norwegian activity in Chile seems to be of a composite nature. Due to low labor cost and subsequrent higher food processing possibilities, the produce from Chile has higher value added than the Norwegian.produce. According to the consultancy firm Kontali Analyse, the Chilean production consists of 96 percent filets and 4 percents basic preparation of the fish, whereas this ratio is onøly 16 percent filets in Norway (Liabø 2003). With the ability to export filets, the firms may more easily export to the North American market.

The massive increase of FDI into Chilean fish farming has also had its downsides. Indeed, the fish farming activities will from now on expand to the densely populated southern regions of the country (*Intrafish* 2000). But according to Barret et al. (2002), the activities thus far were located in areas where the local population had previously been self-sufficient small unit fishers. These have now abandoned their traditional occupations and taken up occupation in the fish farms. As with many industrialization processes the prevalent social structure has received a massive and definite blow. There are figures indicating increased levels of social problems in the communities, as well as environmental problems in the form of pollution from the fish farms (ibid.). Indeed, these consequences are not the result of Norwegian FDI alone, but the phenomenon deserves attention, and the domestic activities of the industry should in future studies of this type be seen in relation to its overseas activities in a way we do not have the resources to pursue here.[16]

When the first fish farms were established in Norway, the whole industry was very much based on entrepreneurship and enthusiasm. It has grown to be one of the most important industries in the country since it is away from the urban centres, it does in addition create much needed jobs in rural areas. A law about "one owner – one facility", which posed a barrier for development, was changed. So was the requirement that local people must have majority of the ownership, and this opened for a number of mergers and acquisitions (Aquamedia 2003). At the present time the trend is that fewer and bigger companies are beginning to control larger parts of the market, and that many companies have varying kinds of co-operation (Fraas et al. 2002; Hansen 2003). By the end of 2001 there were 848 licenses for fish farm, 302 licenses for hatcheries and 28 licenses for parent fish farms (*Fiskeri og Havbruk* 2002).

The Norwegian fish farming industry iscurrently in a difficult period economically speaking. In 2001 and 2002 the prices of fresh salmon and trout dropped by approximately 5% and profitability of the fish sector decreased. This trend seems to continue also in 2003-2004.

The innovation cost intensity (the ratio of expenditures for innovation purposes to turnover) within fish farming is among the lowest of all sectors. The average innovation cost intensity within business in general in Norway was 1.79% of turnover in 1997. For fish farming the figure was 0.76% (Fraas et al 2002: 38). In addition, the input expenditures seem to be overwhelmingly directed with process innovation purposes in mind. More precisely,

[16] For more information on Chile, see e.g. Bjørndal (2002) and Phynel & Mansilla (2003).

according to the innovation survey of 1997, the purchase of machinery and equipment amounted to 68.3% for fish farming, whereas the corresponding figure for manufacturing was 44,90% (Table 3-8).

Table 3-8: Innovative expenditure, 1997, according to purpose

	Fish farms	Manufacturing
R&D within firm	4.17	24.96
Purchased R&D	8.62	7.56
Purchase of machinery and equipment tied to product and process innovations	68.38	44.90
Purchase of other technology tied to product and process innovations	11.91	4.37
Industrial design etc.	2.90	6.45
Competence building tied to technological innovations	2.41	7.89
Market introduction of technological innovations	1.58	3.82

Source: Innovation survey 1997, as cited in Fraas et al (2002: 38).

These statistics do thus fit with observations made elsewhere in the report regarding potentially costly biotechnology-related innovation as not occurring in general within fish farming itself. Fish farms are mainly preoccupied with increasing rationalization of production itself by way of equipment purchases and process innovations (cf. Table 3-9).

Table 3-9: Innovative activity in aquaculture and pharmaceuticals, 1999 – 2001

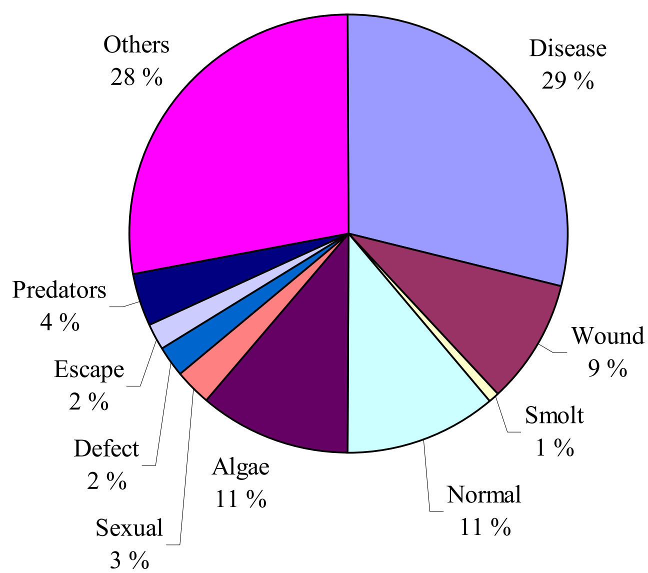
	Fish farms	Pharmaceuticals
Firms in Sample	105	15
Firms with innovation	40	12
Percentage share:		
Product or service innovations	38	80
Product innovations	34	80
Product new for the market	11	33
Process innovations	38	51
Product and process innovations	34	51

Source: CIS3, Statistics Norway

Diseases.

The most vulnerable points in fish farming are related to diseases, algae and jellyfish, physical damages, maturation and escaping fish.[17] Fig. 3-1 shows losses in the production of salmon by cause.

Figure 3-1: Losses in the production of salmon by cause.



In 2002 premature salmon death caused a loss of 30 million fish. There is, as described below, conducted considerable R&D in Norway related to avoiding diseases, including the development of vaccines. One of the major problems for the fish industry is the continuously threatening diseases, caused by various living organisms in the sea. Some of the organisms are the toxic algae. There are several types of toxic algae produced in the sea, some representing a threat for the fish, others being "killer cells" for human cancer cells. By mapping the genetic disposition of a toxic algae one can predict the growth and time when these toxic micro-organisms are to invade the banks and cause massive fish death. One toxic algae, pfiesteria which originates from the US and has so far not been detected in Norway,

[17] This section is from this point and onwards to a large extent based on Dahl-Hilstad (2003).

might be a threat for the Norwegian coast in the future. The algae represents a danger also for humans, infecting the skin and causing severe neurological disorders.

Fig 3-2: Some of the indoor tanks in the hatchery at Urke, Sunnmøre, Norway.

Photo by Anders Dahl-Hilstad

From both health and economic perspectives, it is far more beneficial to prevent a disease from happening than it is to treat the disease after it strikes.[18] Infectious disease outbreaks not only cause losses of valuable fish, they can affect appetite, which reduces the effectiveness of oral therapeutics, and may reduce growth. In addition, survivors may be low-level carriers of the pathogen, capable of infecting healthy fish in the population, and potentially perpetuating the disease cycle. Fig. 3-3 shows the use of antibiotics and production of fish, both in tonnes, in period 1998 – 2000. The use of antibiotics had a remarkable decline in the last decade while fish production increased.

The ability of a fish to develop immunity to a disease by vaccination appears to be dependent on three main factors: (1) the size of the fish; (2) the water temperature; and (3) the method of vaccination. Environment and hygiene can also affect immunity. If fish health is compromised at the time of vaccination, immunity may be impacted. The immune response to vaccination increases with fish size and with increasing water temperature, so timing of vaccination before exposure to a disease is important. Immunity develops better if the

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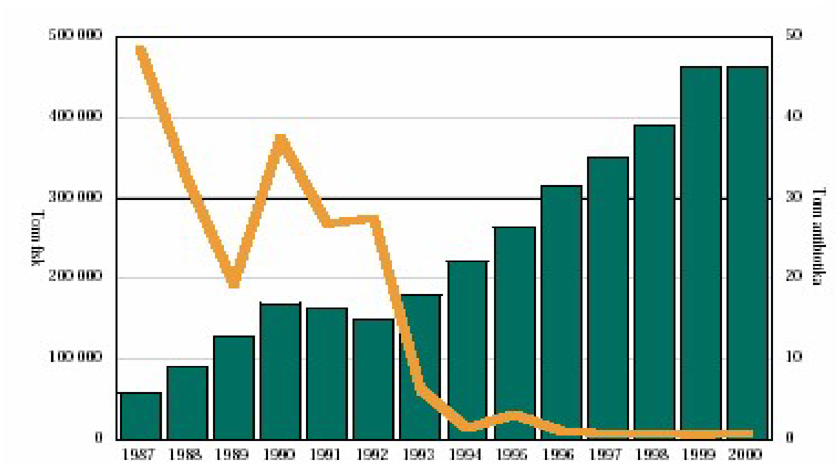
[18] From the perspective of the pharmaceuticals-producing firm, it might be more financial rewards if treatment by way of pharmaceuticals is in the focus. If this might be the case when it comes to humans, it will nevertheless be more benefial to all parties with disease prevention in the case of marine species, since there is small possibility of treating, and then send to the market, fish which have already become sick.

smallest fish weighs over 2.5 grams. When water temperatures are lower than 6°C, it is generally accepted that fish should not be vaccinated by the immersion method, as immunity may not develop. At 8°C, it will take about 5 weeks for immunity to develop, compared to 2 weeks at 12°C.

Fig. 3-3: Use of antibiotics within Norwegian salmon and trout farming 1987-2000



Notes: Use of antibiotics (yellow line) and amount of fish produced (blue columns). The numbers on the left side are the tonnes of fish; the numbers on the right side are the tonnes of antibiotics.
Sources: NMD & Directorate for fisheries, as cited in Ministry of Fisheries (2002).

The most threatening infectious disease in the Norwegian aquaculture industry are furuncolosis, BKD (bacterial kidney disease), IPN (infectious pancreatic necrosis), vibriosis and winter wounds (Wergeland et al 1996). With furuncolosis, the work to develop a vaccine was even harder than it was with cold-water vibriosis, as the bacteria is more complicated, and so are the ways the infection spreads. At a point this disease was also threatening the stock of wild-salmon in Norwegian rivers, but thanks to vaccines and more knowledge of how to prevent contamination, the disease is no longer a serious problem.

Lots of efforts have been used to develop polyvalent vaccines that would protect the fish against more than one disease, as the fish was exposed to several diseases. Tests were done to make sure that the combination of different antigens did not lead to a lower effect on the immune system for each of them than what would have been. Today, the rule is combination vaccines in Norway, and a vaccine can consists of up to six different components. The diseases the smolt is vaccinated against are vibriosis, cold-water vibriosis, furunculosis, BKD, IPN and winter wounds caused by the bacteria M. viscosa. Of these, only IPN is a viral disease.

Vaccine-producing firms in Norway

The three companies to be mentioned as the producers of vaccines in Norway are Alpharma, Intervet Norbio and Scanvacc, and they all have very different backgrounds and history.

Alpharma is a multinational enterprise with a Norwegian majority of shares that is dealing with pharmaceuticals for humans and animals. The company was started in Oslo in 1903 by apothecaries and has been an actor in the fish pharmaceutical market from the 1980s when Alpharma bought a company called Biomed in Seattle that had been dealing with fish vaccines since 1970 (Alpharma 2003). The company has all the time had an active policy when it comes to buying other companies in the US, and as that part of the activities grew big, the company registered on the New York stock exchange in 1994. The same year the firm transferred their parent operations to the USA. Alpharma as a whole has about 4000 employees. Out of these, 70 or 80 are working with fish health, so it is admittedly a minor activity within the overall picture. The firm has production in different places in the world, but the production of fish vaccines takes place in Overhalla in Norway. Its fish health related R&D also takes place in Norway. During the 1980s it had a large market share in Norway. It once the fell because of production problems, but is now growing again.

Intervet Norbio is a part of Intervet International, a multinational enterprise focusing on animal healthcare products for the worldwide veterinary market. These include vaccines, antibiotics and anti-infectives. Intervet International belongs to the Akzo Nobel group. Akzo Nobel is dealing within both human and veterinary pharmaceuticals. Intervet Norbio itself was started in Bergen in 1985 as the firm Norbio by professor Kjell Kleppe and financed by the entrepreneur Eirik Sande, and the firm had from the start its focus on fish vaccines. Professor Kleppe had been the director of the department for biotechnology at the University of Bergen and started the company after he saw the start of the commercialization of biotechnology and recombinant DNA technique in the US. The first employees were all recruited from the University of Bergen, and the company remained closely knit to the university. This gave a strong emphasis on research, and the company did not have any commercial breakthroughs the first years. In 1990, the entrepreneur company pulled out of Norbio because they could not finance it further, but after being “kept alive” by several Norwegian companies, Norbio was sold to Intervet International in 1993. At that point, Intervet International did not have a department for fish health. The acquisition of Norbio was thus complementary to its existing activities, and from 1993 the company also started to make money on the activity. Intervet Norbio is of the opinion that Norwegian capital had a too conservative thinking to see the possibilities in firms like Norbio, and seemed to only keep the company alive until they sold it to foreign actors (interview). Intervet Norbio has not bought companies in Norway since the start, but has bought or built up competence other places. The firm does its R&D for cold-water species in Norway, and is building up the same facilities for warm-water species in Singapore. There are thirty employees in Norway. About 20 of them are doing R&D for new products and have worldwide responsibility for cold-water species, and the rest have the marketing responsibility for Scandinavia. Intervet Norbio indicates that its market share in Norway is about 60%.

Scanvacc is the distributor for Novartis / Aqua Health in Norway. The company was started as a new Ltd. Co. in 1997 and is the youngest of the companies. Aqua Health has been represented in Norway since 1987-1988 through a distributor in Denmark, but got a Norwegian distributor in 1990 when the feed-specialized firm EWOS (see section 3.2.5) took that part. Scanvacc was started by two persons who had formerly been employed in EWOS. The company is not a part of a MNE, and has not acquired any other companies since the start, but owns 50% in an associated local company. It is now Norvartis’ distributor in Norway, Sweden and Finland on marine medicine. The R&D conducted in the company is documentation and testing of vaccines for Norwegian adaptation.

The case of ISA-vaccine development

In order to get a picture of the activities regarding vaccine development we have chosen to focus on a particular case, rather than to try to map all the current diseases and their vaccines. We have chosen to focus on the so called ISA-vaccines.

Firstly, one has to look at what kind of vaccine the producers want to get licensed. The version of the ISA vaccine that the three companies want to license in Norway is what can be called a traditional vaccine. There has been no use of gene technology or other techniques that could make the vaccine in any way controversial except for the fact that the firms wish to vaccinate against ISA, and that has to this date been forbidden in Norway and the EU.

The vaccines in use today are so called polyvalent vaccines. To be able to sell an ISA vaccine the company must be able to include the ISA vaccine in an existing combination. There are two factors that need to be present before it is possible to develop a vaccine. Firstly, one needs the virus, and secondly, the technology to develop a vaccine. Intervet Norbio started a process to characterize the virus and identify the gene that produces it at the same time as the firm started its traditional research. It is difficult to protect an entire virus by patent, and so the firm has to become either the only one to produce a vaccine, or be paid by others that produce vaccines. It is easier to patent a gene and then use this gene to produce a protein that is killed and used inside a vaccine. This way, one uses the recombinant DNA technique, and uses a GMO in the process to produce the vaccine, not in the finished product. By using this technology it is cheaper to produce the vaccine.

Alpharma stresses that there are two kinds of traditional vaccines; those that give protective immunity, which means that the fish does not get infected, but still will be a carrier of the virus, and you have the ones that gives sterilizing immunity which means that the fish does not get sick, and can not be a carrier of the virus. The ISA vaccine has to be of the second type and give a sterilizing immunity. Even though the national plan for fighting ISA opens for some vaccination, the goal is still eradication of the disease and hence the vaccine needs a sterilizing effect.

Scanvacc’s ISA vaccine is produced in Canada by Aqua Health and is based on the one that is on the market there. The ISA component for the two countries is the same, but the vaccine is adapted to Norwegian conditions. The other components of the vaccine (as it is a polyvalent one) are adapted to the Norwegian market. Even though the vaccine is especially adapted to Norwegian conditions, it is also meant for the Faroe Islands, as Scanvacc is also distributor for that area.

The three producers in question are as of 2003 in a situation where they know what to expect from the vaccine they have developed. They have all done laboratory tests, and the next step on the way would be to conduct clinical trials. In order to do these trials, they need permission from the Norwegian Animal Health Agency. There is a possibility that the producers will not get a permission to conduct clinical trials because there according to current rules have to be a precedent vaccine in order to conduct trials. However, there is no existing licensed vaccine, and the new vaccines will not be licensed because the clinical trials have not been conducted. This can thus be seen as a kind of catch 22-situation.

As for the demand side in the system, there have so far been three outbreaks of ISA in Norway during 2003 only, and the fish farmers do seem to want a vaccine. They can only wait for the decision of the authorities to see if vaccination will be a real opportunity. The relationship between the producers and the demand side has changed over the years. The trend today is, as described previously in this report, towards fewer and bigger companies as opposed to the situation when the industry was starting up. This has also changed the relationship between the vaccine producers and the fish farmers, and what the fish farmers demand from the producers. Bigger companies have more knowledge, and it is not unusual for such big companies to have veterinarians on their staff. Also, even though it is not allowed for the vaccine producers to market their products directly towards the users, it has happened that larger companies have invited the three producers to meetings and had them give estimates of the price and the quality of their products, before deciding which supplier to go with. The producers are aware of what the new situation demands of them, and one of the vaccine suppliers stated that the fish farmers are now also demanding knowledge. The products the producers offer is quite similar, and it is important to build a relationship of trust between the producer and the user of the product. When a fish farmer chooses a producer, he or she also knows that they are not only getting the product, but also the knowledge they might need.

3.2.5. Marine management I: the case of feed development.

During its life cycle salmon changes between living in fresh water and salt water.[19] After the early period when the fish grows to about 75-100 grams in fresh water, the smolt is

[19] This section is based on Johansson (forthcoming).

transferred to the salt water sea. The Norwegian conditions in the sea are optimal for salmon breeding due to topography, temperature, streams and salt content of the water. In the early 1980s, salmon feed was produced of melted fish, vitamins, minerals and colour additives, while in the last decade a ready-to-use dry feed has been used.[20] The dry feed contains all vitamins and nutrients (protein, fat, carbohydrate) that are essential for the normal development of the fish. The suppliers of fish feed produce different kinds of feed: Starting feed, transfer feed and growth feed. Some products have additional qualities – they are functional feed (or health feed). Some of these products contain components that could be understood as biotechnological products, or they have been produced through biotechnological processes.

One example is the Nutreco/Skretting product "Response" in which beta glucan is added. This chemical substance is produced through using yeast (fermentation). Skretting is cooperating with the Tromsø company Biotech Pharmacon ASA mentioned above, in order to develop new applications of this substance for use on humans. Another example is the EWOS product "Boost" which contains nucleotides (i.e. chemical substances that build up the macro molecule DNA), a substance produced by the Swiss company Chemofarma, also through fermentation. The control of growth and sexual maturity can also be achieved by genetic engineering. As it is pointed out in strategic plan for FUGE, in addition to research on reproduction and resistance against diseases, the most major field of interest is growth control. So far, there is a UK research group doing progress in this area.

The feed industry is undergoing a rapid development, not only as to the composition and ingredients, but also as to the distribution of the feed in the water. Nowadays, the manual distribution is replaced by automatic distribution where ICT is employed to indicate the current needs of feed. The automatic feeding system facilitates more accurately the amount of feed to be thrown into the water and diminishes the negative environmental impact the residue feed fallen to the bottom represents.

Under optimal conditions the salmon grows relatively fast. The weight increases from 100 grams to ca 3 kilos in one year. The negative consequence of fast growth is an early sexual

[20] Extruded dry feed was introduced by Skretting in the early 1980s. Today it constitutes ca. 97 % of the market (Waagbø 2001).

maturity, which leads to deterioration of the quality of the meat. Various strategies have been employed in order to regulate this maturing process, like feeding frequency and manipulation of daylight length during the dark season. The main idea behind these strategies was to control the energy status of the fish and the result was positive: the share of sexually mature fish diminished, especially after using the lighting method.

3.2.6. Marine management II: the case of genetics-related R&D.

One firm within genetical R&D was dissolved in the 1990s, whereas there are currently two firms active. The defunct firm, Marine Genetics, conducted research into genetics including experimental copying and subsequent implantation of the salmon's own growth hormones. The firm was, however, a subsidiary of a larger firm, and research dicontinued when the mother firm Selmer Sande went bankrupt (*Norsk Fiskeoppdrett*, No. 7, 1999). Currently the active firms include GenoMar ASA and AquaGen.

GenoMar ASA (previously BioSoft AS) was founded in 1996 by professor Øystein Lie from the Norwegian Veterinary Institute. The firm aims at becoming one of the world leaders when it comes to developing and commercializing broodstocks and provide genetic systems. Sub-groups of products are, firstly, tilapia seed, GenoMar Supreme Tilapia™. The firm runs GenoMar runs research projects where the main goal is to identify genes controlling salt water tolerance in order to develop tilapia strains which perform well in brackish water environments. Although starting out originally as a business concept focusing on the local salmonid species, the firm has thus evolved into concentrating exclusively on a species alien to Norwegian aquaculture environment, the tialpia. The firm is thus an interesting case of a busines idea emerging form the overall aquaculture environment, whereas the present activities are directed to overseas sites rather than to local aquaculture customers.

Secondly, the firm develops breeding technology assisted with DNA fingerprinting customized to customer requests. Thirdly, a patented DNA fingerprint based concept called GenTrack™ has been developed for the purpose of veryfing the origin of seafoods. The firm has nine employees in Norway, nine in the Philippines, and seven in the People's Republic of China (GenoMar 2004)

AquaGen is a breeder of salmon based on systematic selection. Approximately 10 percent of the firm's clients specify in detail the specific design, such as e.g. amount of fat, colkour of meat or shine of coat. In 2001 the firm establisged a Chilean subsidiary called Gentech (*Havbruk* January 2001) .

4. Conclusions and policy implications

Several studies have attempted to approach biotechnology as "a whole", and analyze the various sub-sectors which have applications of this technology (biopharmaceuticals, agriculture, aquaculture, etc.) in one and the same study (see e.g. Bartholomew 1997; Mangematin et.al. 2003). Such an approach may be feasible on a, literally, highly aggregate level, in order to assess whether there is a national system for biotechnology at that level. However, and as the same authors also point out, biotechnology is essentially a broad technological approach, and there may be great variations when it comes to innovation system features according to what industrial sub-sector one is referring to.

This seems to be particularly the case with marine technology. Aquaculture, for example, is a huge and complex sub-sector by itself ranging from public and business actors not involved at all in aspects relevant to biotechnology (transporters, equipment suppliers, and for the most part even the fish farmers themselves), to the actors moderately involved (feed producers), and onwards to actors heavily involved in biotechnology activities (advanced breeding techniques providers, fish health solution providers).

These concluding remarks are therefore not aiming at an aggregate and generalized level, but sticks to the division between marine biotechnology sub-areas outlined previously in the report. We will, however, discern between drugs and material developers on the one hand, and aquaculture suppliers on the other hand.

Although comprehensive reflections are difficult to make based on the recent date of many or most of the described developments, as well as based on the rather limited amount of documentation behind this report, we will tentatively suggest some observations and policy implications. We choose to formulate the observations and discussion in the form of questions or hypotheses, which are then followed up.

> Scientific exploitation of available material: There is in quantitative terms a considerable amount of public sector research and education within marine topics. In recent years, funding has increased substantially. But is it the case that basic research

in marine biology etc. is still in a transition stage, where there is still predominantly a preoccupation with topics belonging to "the past age" of resource management related to conventional catch fisheries?

The issue at stake here is the relationship between the repeated policy statements concerning a comparative advantage consisting of available scientific input factor on the one hand, and the commercialisation of the rich and available arctic biodiversity on the other. Despute the existence of competence within marine biology in broader terms, this inter-relationship does not necessarily exist already, but may take its time to develop. One can also ask whether the visions as formulated within present day policy initiatives are feasible either in the medium or long term perspective if there is indeed a persisting divide between traditional, resource based disciplines and disciplines more focused on biotechnology. Needless to say, resource based disciplines will still have immense importance also in the future. However, there may in a case like this be path dependencies at work where new perspectives may experience entry difficulties. If this problem occurs and persists, the policy statements regarding comparative advantage lose some of their momentum.

Forms of organization: Two of the most successful examples within marine based drugs and enzyme development were predominantly sponsored by big business, more precisely the petroleum industry, rather than by public R&D support alone. Is this feasible also in the future?

The fact that Pronova Biocare and Biotec Pharmacon were supported by the petroleum industry is interesting and admirable in itself. We have not found any similar cases in the other parts of the biopharmaceutical as described in Vol. I. However, it is not feasible to expect that the petroleum industry will continue to sponsor such projects also in the future, and this leads to the question of the appropriate organizational form of start-ups within the drugs and materials segment. Facing international competition, it might be expected that it will take considerable basic research efforts on marine organisms including full genome mapping before it becomes feasible to identify promising areas and, later, develop further with the aim of approaching the market. In such a context, it will be necessary to follow up on the example of "virtual" companies such as Protevs in Bergen and Hepmarin in Ås, where the public investment and interest is considerable. Needless to say, purely private initiatives should be welcomed as well, but with the early stage this type of research is in it seems more feasible that a more solid basis is needed before substantial private investment may be expected.

> Should Norwegian policy on marine biotechnology be more targeted, and favour certain relevant segments, in order for these segments to become more competitive worldwide?

The author(s) of this report lack the technical competence needed in order to identify particularly promising areas of research. In more general terms, however, it seems to become necessary to move onwards from the policy statements of the late 1990s and early 2000s consisting of rather general statements on presumed comparative advantage, towards more specific areas of targeting. There are, for example, already dozens of firms worldwide specializing in the industrial commercialisation of various aspects of chitosan. Within the segment of arctic species, research targeting of a more precise nature either on domestic or international and collaborative terms could warrant for a higher probability of success in the long term.

Turning to issues more specific to the two aquaculture-specific sub-areas regarding aquaculture support functions and environmental management more at large, we would like to ask in similar terms whether:

> Should Norwegian policy regarding aquaculture be more targeted, and favour certain relevant segments, in order for these segments to become more competitive worldwide?

Favouring one sub-sector in front of another has always been a heavily debated issue, both in the domestic Norwegian context and internationally. However, there seems to be a series of unresolved problem regarding the balance between animal health issues and environment, which could warrant for some type of procurement systems, since one might assume that the fish farming industry itself might want to purchase only the necessary medication, and not be involved in larger and long term issues longer than absolutely necessary. The eventual success of such enlarged projects could benefit not only the industry in a narrow sense, but could perhaps be adapted to other contexts.

One hypothetical example is the dilemma between applying a vaccine which might be efficient in its own right, and eventually absolving from doing so since it might pose a serious problem if a large number of vaccinated fish escape into the natural eco-system. The costly, in itself, development of safer and less risky alternatives would be beneficial both to industry and the biotech suppliers in Norway. They might even be part in public assistance projects overseas wherever applicable. Likewise, the genetic sequencing of fish genes in order to establish better possibilities for classical breeding techniques, as well as provide foundation for further basic research, is sorely in need in many countries. The breeding and gene sequencing research in Norway could perhaps get a boost by being coupled to such kind of international collaboration or aid in the wide sense.

> In order to increase biotechnology content and innovation, should fish farmers as well as fish export companies be targeted in some way or the other?

We have shown that there are certain traits with the fish farming industry, such as a high level of division of labour between the different parts of the system and extremely low expenditure on innovation activities. If it is the goal to increase the involvement of industry in the basic research development of new species for fish farming, for example, there is a need to target the firms in some way or the other. It is doubtful whether firms will diversify as a result of a particular policy. At the same time, if the Norwegian government sets as a requirement for the use of Norwegian shores the participation in some kind of development programme, there is an immediate risk for increased levels of transfer of activities to elsewhere. This area is, in other words, a dilemma. But we have seen that there is a large amount of marine resource related research going on in the public sector, and some measures in the direction towards a type of created, demand-driven innovation resulting from increased levels of interaction between the funders/producers of the research results and the potential users could be contemplated.

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Appendix 2: Overview of main public aquaculture research organisations in Norway.

Universities and colleges	R&D Institutes
University of Bergen Sars International Research Centre Institute for pharmacology Institute for Molecular Biology Institute for Fishery and Marine Biology Centre for Studies in Environment and Resources Zoological institute	Foundation for Research in Society and Business (“Stiftelsen for samfunns- og næringslivsforskning “) Institute for Research in Aquaculture (“Institutt for akvakulturforskning AS “) Norwegian Institute for Agricultural Research (“Norsk institutt for landbruksøkonomisk forskning (NILF)”)
National University of Science and Technology Trondheim Institute for Natural History - Trondhjem biological station - Zoologisk avdeling Institute for Technical Cybernetics Botanical Institute Zoological Institute	Norwegian Institute for Food Research (“Norsk institutt for næringsmiddelforskning (MATFORSK)”) Norwegian Institute for Research in Natural Sciences (“Norsk institutt for naturforskning (NINA)”) Norwegian Institute for Water Research (“Norsk institutt for vannforskning (NIVA)”)
University of Tromsø Norwegian College of Fishery Science Institute for Marine Biology and Freshwater Biology Institute for Social Studies and Marketing Institute for Economics Institute for Marine Biotechnology Institute for Aquatic resources and Environmental Technology	NORUT Finnmark AS Heering oils flours research institute (“Sildolje- og sildemelindustriens forskningsinstitutt”, part of Fiskeriforskning from 1 September 2002) SINTEF Fisheries and sea Ranching (“SINTEF Fiskeri og Havbruk AS “) Institute of Oceanic Research (“Havforskningsinstituttet “) Institute for Veterinary Studies (VESO)
Norwegian Agricultural University Institute for Domestic Animals Institute for Technical Studies	Directorate of Fisheries Institute of Nutrition (“Fiskeridirektoratets ernæringsinstitutt” (from 2003: “Nasjonalt institutt for ernærings- og sjømatforskning”) Møre Region Research (“Møreforsking”)
Norwegian Veterinary University Institute for Biochemistry, Physiology and Nutrition Institute for Pharmacology, Microbiology and næringsmiddelhygiene Institute for Morphology, Genetics and Marine Biology	NORCONSERV – Institute for Fish Processing and Conservation Technology (“Institutt for fiskeforedling og konserveringsteknologi “ Nordland prefecture research (“Nordlandsforskning”)
Regional College Bodø Department of Fisheries and Science	Norwegian Institute for Fisheries and Marine Research (“Norsk institutt for fiskeri og havbruksforskning AS” aka “Fiskeriforskning”))
Regional College - Sogn og Fjordane	Aquatic Research (“ Akvaforsk”)

Source: FoU ressurser innenfor havbruk 2001, NIFU skriftserie nr.4/2003, p. 38 (translated).

Appendix 2: Overview of selected marine biotechnology and related firms in Norway.

Category		Firm	Product(s)	Address
Developing novel drugs	Drugs for humans	Pronova Biocare as	Omega 3 based products	www.pronovabiocare.com
		Biotec Pharmacon ASA	Bioactivite compounds & DNA modifying of marine based enzymes	www.biotec.no
		Hepmarin AS	Anticoagulants based on marine products. Firm spun off from the science park BioParken.	Ås.
		Thia Medica AS	Modified fatty acid (TTA) for metabolic disorders. University of Bergen spin-off.	Bergen
	Fish health	Alpharma AS	Speciality antibiotics. vaccines	www.alpharma.com
		Intervet Norbio AS	Fish health related 10 products in development, 10 products on market. Vaccines and endocrine products	www.intervet.com
		Scanvacc	Development and sale of health products for fish farming	www.scanvacc.com/
New types of composite materials, biopolymers and enzymes for industrial use		FMC Biopolymer AS (subsidiary of MNC FMC Biopolymer)	Biopolymers (alginates and carrageenans) processed from seaweeds and microcrystalline cellulose processed from specialty grades of pulp.	www.fmcbiopolymer.com
		Ami Go As	Splitting fish protein into free amino acid by using enzymatic methods.	www.fortuna.no
		Aqua Biotech Technology AS	Enzymes	5640 Eikelandsosen
		Promar Aqua AS	Algae production for medicinal use in conjunction with industrial area and planned site for lobster	
		Maritex AS (subsidiary of Tine dairy products)	Research on marine ingredients for use in dietary supplements and fish and animal feed. Seems to include former Tine subsidiary Tine Biomarin (est. 2001)	www.maritex.com
		Napro pharma AS	Develop products from fish oils and omega 3 concentrates for sale to the nutricitical industry. Bulk marine and vegetable oils for pharmaceutical use.	http://www.napro-pharma.no/sider/index2.html N-6270 Brattevåg

Composite materials etc. (cont.)		Natural ASA	Licensing company selling solutions for commercialising of marine products based on fatty acids mainly for use in dietary supplements	http://www.natural.no/
		ProBio Nutraceuticals AS	Production of customised food additives based on fish oils mainly for dietary supplements and nutraceuticals	www.probio.no Tromsø
		Firmenich Bjørge Biomarin AS	Natural seafood extracts for production of flavoring materials for the food, beverage and pharmaceutical industries. Bjørge Biomarin AS bought by Swiss firm Firmenich in 2002.	N-6057 Ellingsøy
		Biohenk (Subsidiary of MNC Cognis**)**	Fish waste treatment. Production of chitosan from prawn shells. Sold mainly to the cosmetic industry.	
		Primex Biochemicals (subsidiary of Primex ehf, Iceland)	Chitin derivatives and specialty marine proteins. E.g. product ReduSan. Also supplies partially hydrolysed marine proteins for various applications in the food and feed markets. Primex is the successor of Genis ehf, which acquired the Norwegian company Primex Ingredients ASA in September 2001.	Siglufjordur, Iceland / Haugesund
		Sigtun AS	Bioacitve molecular products based on mussels (holding company)	
		Biopharma AS	Dietary supplements based on marine ingredients (import and sales)	
		Norferm DA	Development of bioprotein production technology	www.norferm.com
		Biosentrum AS	Contract fermentation	www.biosentrum.com
Safety of aquaculture and fisheries/providing new techniques for management of marine environments	Genetics	Aqua Gen	Breeding based on genetics	www.aquagen.no
		GenoMar	Genetic enhancement of aquatic species and DNA profiling for tracing of fish origin	www.genomar.no
	Feed	Nutreco / Skretting	Feed producer	
		EWOS	Feed producer	
		BioMar AS	Feed producer	
		Polarfeed AS	Feed producer	

Aquaculture-related (cont.	Misc.	Biosense Laboratories A/S	Vitellogenin (Vtg) ELISA Kits, for quantification oestrogen effects in fish, etc.	www.biosense.no
		Bionor AS	Diagnostic products for human and veterinarian medicine including aqua culture.	www.bionor.com
		Promar Aqua AS/Intravision	Photosynthesis bioreactor for production of microalgae.	

Sources: List of recipients from the R&D tax alleviation programme Skattefunn, membership list for Norwegian Bioindustry Association, industry publications such as *IntraFish* and *Norsk Fiskeoppdrett*, field notes, and firm home pages. Thus we do not claim that the list is literally comprehensive, but it should on an indicative basis cover a great majority of commercial marine biotechnology activities.