The Netherlands

Henk C. van der Plas

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1.8. THE NETHERLANDS

Henk C. van der Plas

In September 1984 Professor Schilperport, then Chairman of the Programme Committee on Biotechnology, PCB, suggested that in the 1990s the Netherlands might be the biotechnology delta of Europe. Is that fiction or reality?

The Netherlands posses an industrial base of about 100 biotechnology firms, together providing an R&D potential of 1,100 manyears (in 1985). Sales of traditional biotechnology products in the dairy, brewery and antibiotics industries accounted for sales of about US$4 billion. New products such as recombinant vaccines and diagnostics based on monoclonal antibody technology are contributing to 1987 sales of about US$40 million.

A few major companies dominate biotechnology in the Netherlands. These have a base in traditional biotechnology and have rapidly included new technology in their ranges of competence. Many, much smaller companies have emerged recently, partly because of the relatively easy access to investment capital.

Figure 1 summarises the scope for biotechnology R&D in the Netherlands. The role of the major companies is clear.

Because of the small size of the country and the initiative of the government in pushing activities in biotechnology, there exists a solid network of contact and communication among all Dutch biotechnologists, in industrial, university or government laboratories.

The standard of excellence in Dutch universities is among the highest in Europe, and although there was considerable displeasure some 7 years ago when the government first sought to stimulate a productive orientation, almost all would now admit that the scheme has been successful.

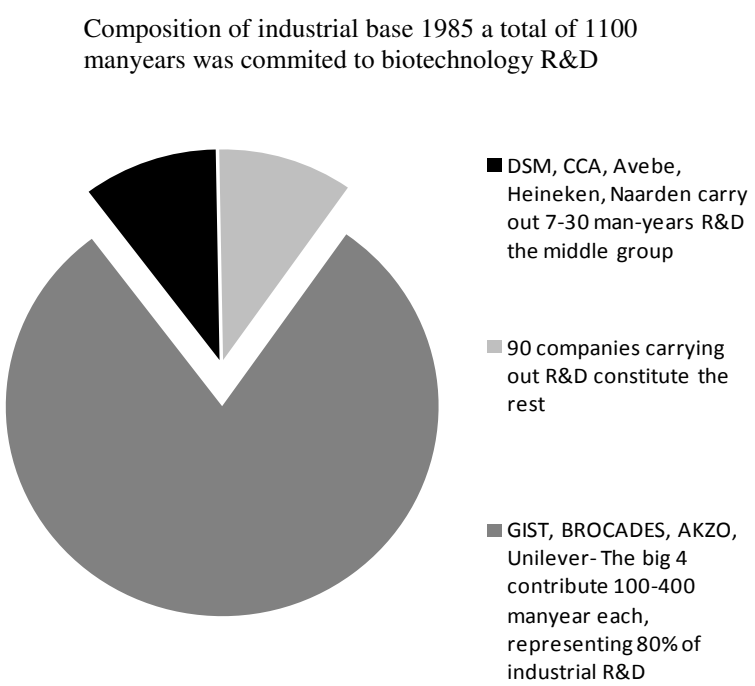

Fig. 1. Scope for biotechnology R&D in the Netherlands

The small size of the country cannot hide the fact that it plays host to some of the more prominent multinationals. The financial power of big companies, combined with experience and marketing know how has made it possible to exploit the opportunities in biotechnology.

Small is effective for the Netherlands. Communications are no problem as all locations are geographically close.

The government has made biotechnology a priority area, not only because of the solid industrial base, but also because biotechnology provides fast growing market opportunities in many industrial sectors.

The Role of the Government

The government launched its Innovation-Oriented Biotechnology Research Programme in 1981. This formed part of a series of similar such

programmes in a number of strategically critical areas including: membranes, polymers, composites, carbohydrates, engineering ceramics etc. The primary goal of these innovation oriented research programmes, IOPs, is to stimulate research in universities and institutes. The goal is three pronged, seeking:

- to stimulate research.
- to structure the knowledge infrastructure through division of tasks, co-operation and market orientation.
- to set up a communications network.

Let me explain these three points. Stimulation of biotechnological research at universities and institutes is being accomplished by provision of an extra US$20 million between 1981 and 1990. The money is shared out by a high level body, the Advisory Committee on Biotechnology, ACB, which, although government appointed, works at arm's length from the government. Its membership includes representatives of both industry and research institutes. The indirect, co-ordinating, effect of this extra financial stimulation is, in my opinion, even greater than the direct impact.

The Advisory Committee on Biotechnology seeks to realise the entire threefold goal simultaneously. As in some countries, government funded university research in the Netherlands is being trimmed, owing to budget constraints. The division of tasks is therefore an indispensable element for structuring the knowledge infrastructure (e.g. to avoid overlap).

Biotechnology is a multidisciplinary science. Co-operation between research teams is a sheer necessity, because only integration of knowledge can produce practical applications. The third element of restructuring the knowledge infrastructure, finally, is more market orientation. Extensive consultation with industry was found to be a simple and effective way of learning exactly what the market needs.

An inventory of the wishes and needs of industry, as regards both research objectives and research teams, served as a basis for this industrial orientation. The inventory was made through confidential interviews, the results of which were generalised. This guaranteed an open industrial orientation.

The third goal, that of building up a *communications network*, is vital for the rapid growth of a new technology, which cannot develop without dose co-operation between everyone concerned.

Central to the IOP network is the Advisory Committee on Biotechnology, ACB, which co-ordinates the overall stimulation of the four sub-programmes on Biotechnology under the supervision of four separate Programme Committees, PCs. Each of the four PCs receives money from the Ministry most closely involved.

The ACB together with the four Programme Committees has also succeeded in creating the conditions for good fines of communication between research institutes, industry (including investors) and government.

In the first stage of the IOP, from 1981 through to 1984, financial stimulation was used to raise the level of biotechnological research on a broad scale, while building up a communications network. At the same time inventories were taken to determine the direction of the infrastructure structuring.

In the second stage from 1985 to 1990, structuring is being selectively programmed and anchored in the infrastructure, so that industry will be able to continue making optimal use of the government funded knowledge infrastructure after the programme has ended.

The following tables show the range of activities encountered in government funded institutes and universities.

***Table 1*. The Major University Biotechnology Centres in the Netherlands.**

Centre	Activity
BDL, Biotechnology Delft-Leiden (Technical University Delft & State University Leiden)	Incomplete oxidations Plant cell biotechnology Yeast physiology/genetics Environmental biotechnology control Bioreactor design and downstream processing
Agricultural University Wageningen	Biocatalysts Food and animal feeds Waste and environment Plant cells Animal cells
BCA, Biotechnolog Centre Amsterdan (Free Universit Amsterdam & University of Amsterdam)	Opimisation of product formation by micro-organisms (yeast & prokaryotes) Plant biotechnology Monoclonal antibody production Enzymology
State University Utrecht	Vaccines Peptide and polypeptide hormones Monoclonal antibodies
State University Groningen	Fine chemicals and stereo specific reactions Development of host-vector systems for industrial micro-organisms Biological oxidation, biodegradation of waste
Chemical	Optimisation of dairy micro-organisms

Table 2 **Some of the Important Biotechnology Research Institutes in the Netherlands**	
Institute	Activity
Plant Biotechnology	
Wageningen: SVP, ITAL	Genetic engineering for plant breeding
ITAL	Secondary metabolite production for high grade chemicals
IVT	Horticulture
IPO, IVT	Disease and pest resistance
Baarn: CBS	Central Bureau for Mycology
Agroprocess Biotechnology	
Wageningen: Sprengen-IBVL	Processing of waste flows
IMAG	Treatment of manure
Ede: NIZO	Dairy production and processing
Groningen: NIKO	Carbohydrates
Zeist: TNO	Food and animal feeds (incl. biocatalysus and bioprocess technology)
Animal Cell Technology	
Lelystad: CDI	Vaccine and diagnostics development
IVVO	Livestock feeding/nutrition
Wageningen: ITAL	Malaria control by insect genectics
Zeist: IVO	Animal production
Medical Biotechnology	
Amsterdam: CLB	Blood/blood factor research tissue culture
NKI	Cancer research
Bilthoven: RIVM	Human vaccines and other biological
Rijswijk: TNO	Monoclonal antibodies for diagnosis/therapy/research rDNA technology
Environmental Biotechnology	
Amsterdam/Delft: TNO	Fermentation and bioprocessing recycling, purification, membrane technology
Bilthoven: RIVM	Microbiological soil and water treatment
Lelystad: RIZA	Waste water research

Since 1983 the Dutch government has encouraged industry to participate in ambitious R&D programmes. Two forms of subsidy have backed up this encouragement.

- the INSTIR subsidy scheme
- case by case assessment

INovation STImulation Regulation, is a scheme which offers wage support for R&D. Given the massive cost of wages in modern industry this incentive dramatically lowers cost thresholds and has been provided for a number of promising technologies, including biotechnology.

Although university collaboration was not a precondition of these subsidies, it is a testimony to the establishment of the communications infrastructure that, in practice most projects were carried out in collaboration with universities or institutes.

The recent economic upturn has made R&D financing much easier for companies, who are now less in need of government support. Since 1987 the Dutch government provides incentives only for technologies in which the support policy results in the highest added value.

Biotechnology is one of the four high tech areas that continues to benefit from public support. The technology policy enabling the knowledge infrastructure through the IOP is being followed up in the form of a programme policy concerned directly with industry.

At this stage the goal is to increase the number of firms engaged in new biotechnology operations from 10 or 20 to 100! More than 100 potentially promising firms that we now have are being prevented from achieving high-tech production in the near future, not so much by lack of money, but by a low level of in-house research activity.

Subsidies do not play major role in the government's programme policy, although they do perform a valuable supportive role. The programme for the 100 companies target covers a number of synergic and mutually complementary activities.

Information and Contact

A vital factor in pulling firms across the threshold towards new technologies is information. This part of the programme is already in full swing, with the publication of booklets and a biotechnology magazine in Dutch. Printed information does not suffice. Personal contacts through consultants paid for by the Economic Affairs Ministry often produce better results. The consultant acts as a broker between industry, the knowledge infrastructure and government.

IOP Biotechnology

Already discussed in the earlier part of this presentation.

Stimulation of Industrial R&D Projects

An important criterium for selection is co-operation with a university or institutional research group. This industrial stimulation is therefore closely linked with the IOP stimulation.

Establishment of New Companies

Can foreign companies be persuaded to set up in the Netherlands, as a consequence of providing the appropriate infrastructure? We have been successful, as the establishment of subsidiaries of the American biotechnology firms, Centocor, Mogen International, Promega and recently EuroCetus demonstrates.

Education

Without suitably skilled manpower, no innovation is possible. We are busy setting up a postgraduate training facility for biotechnology engineers, a joint initiative of Delft and Leiden.

International Co-operation

For a small country like the Netherlands, cross frontier co-operation is important, particularly within the context of the European Community, EC, and EUREKA. Non-European collaboration also receives dose attention from the government, particularly the third world countries. The Netherlands have initiated biotechnology collaborations with Indonesia, India and Thailand.

Optimising the Chances for Success

General policy actions relating to the approval of biotechnology products, patent matters, supplies of cheap raw materials for the fermentation industry and last but not least – social acceptance.

The Dutch government is working for industrial innovation in biotechnology along these lines.

What Has Been Achieved?

A number of products have emerged from the Dutch Biotechnology initiatives. The following are just a sample that illustrates the breadth and potential of the Dutch biotechnology enterprise.

- *Anaerobic purification of waste water:* a co-operation between universities, TNO and Gist-Brocades
- *Development of a vaccine against diarrhea in calves and piglets:* a co-operation between RIVM and Amsterdam University.
- *Pregnancy test using monoclonal antibodies:* Organon
- *Preparation of D I L amino acids by enzymatic separation of D, L mixtures:* Dutch States Mines, DSM.
- *Production of aspartame:* DSM, Toyo Soda
- *Biofilters for air filtration, production of chymosin with rDNA technology:* Gist-Brocades, NIZO

Many other products and processes are well on the way to realisation. The last table gives evidence to support the assertion that growth in biotechnology will be gradual, but steady. At this point I return to the claim that The Netherlands might become a Biotechnology Delta in the 1990s. It is still premature to say that this is more than fiction, but we are working hard to create a really strong base for industrial biotechnology in the next decade. We are full of confidence and so far, if I may say so, we have not been unsuccessful!

I hope this introduction to Dutch biotechnology has roused your interest and that it may lead to the next step of entering into dose co-operation with Dutch partners. The Netherlands is ready for it.

For anyone wishing to learn more about Dutch biotechnology, a highly informative and illustrative brochure can be ordered, as well as a list of names and addresses of Dutch firms and institutes active in the field.

Table 3 Biotechnology Sales for Various Industries: (figures in millions of Guilders)

Industrial sector	Total	Biotechnology sales		
	1982	1985	1990	1995
Fine Chemicals Human & Veterinary	6500	460	555	655
Health Care	2500	750	1000	1350
Food and Beverages	64000	8500	9400	10800
Equipments and Instrumentation	13000	275	310	350
Engineering Contractors	1500	90	160	210

Source: CIVI