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BIOTECHNOLOGY FOR CLEAN INDUSTRIAL PRODUCTS AND PROCESSES

Towards Industrial Sustainability

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ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

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Vers un développement industriel durable

FOREWORD

Biotechnology for Clean Industrial Products and Processes: Towards Industrial Sustainability is the report of an *Ad Hoc* Task Force of the OECD Working Party on Biotechnology. It was approved by the Working Party's 6th Session on 24-25 February, and by the Committee for Scientific and Technological Policy on 10-11 March 1998. It continues the OECD's review of environmental biotechnologies which began with *Biotechnology for a Clean Environment* (1994) and included workshops in Tokyo (1994), Amsterdam (1995) and Mexico (1996), but also opens the door to major new efforts to improve industrial sustainability in and outside the OECD.

Industrial biotechnology has emerged into a world where environmental sustainability has become a global concern. The report illustrates how modern process biotechnologies can address this global concern, and how they are penetrating industrial operations in many sectors. It identifies environmental and economic advantages over other technologies, as well as technical and other bottlenecks. It also emphasises that industry and governments must act together to respond to the challenges of industrial sustainability through biotechnology.

The *Ad Hoc* Task Force was chaired by Alan Bull (United Kingdom), with co-chairs Barry Marrs (United States) and Ryuichiro Kurane (Japan). This team, together with Wulf Crueger (Germany), co-ordinated the drafting work, supported by the Secretariat, where the responsibilities were with Salomon Wald and Tadashi Hirakawa.

The report was written by seven chapter co-ordinators – Chapter 1: A. Bull (United Kingdom), Chapter 2: B. Marrs (United States) and H. Doddema (Netherlands), Chapter 3: R. Kurane (Japan), Chapter 4: W. Crueger (Germany), Chapter 5: B. Dixon (United Kingdom), Chapter 6: V. Aidun (Canada) replacing D. Mahon (Canada), Chapter 7: all.

In addition, *Ad Hoc* Task Force members made essential contributions, particularly R. Atlas (United States) as scientific and policy expert, and M. Griffiths (United Kingdom) as assistant to the chair.

The assistance of many other contributors, including industrial companies, is gratefully acknowledged. Many are mentioned in individual chapters of the report.

Particular thanks are due to the European Commission (DG XII), and to the governments of Germany (BMETF), Japan (MITI) and the Netherlands (Ministry of Economic Affairs) for their generous voluntary contributions to the financing of this report.

The report is published on the responsibility of the Secretary-General of the OECD and does not necessarily reflect the views of the OECD and all its Member countries. In addition, it must be emphasised that the mention of industrial companies, trade names or specific commercial products or processes, does not constitute an endorsement or recommendation by the OECD.

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EXECUTIVE SUMMARY

Industrial biotechnology has come of age. Improved industrial sustainability through biotechnology, the focus of this report, addresses many global environmental concerns. Biotechnology has clear environmental advantages and is economically competitive in a growing number of industrial sectors. It enables reductions of material and energy consumption, as well as pollution and waste generation, for the same level of industrial production. Continued technical innovation, including that based upon recombinant DNA technology, is vital for the wider utilisation of biotechnology by industry. Moreover, joint government-industry action is needed to underpin the development and use of clean industrial products and processes.

Biotechnology for Clean Industrial Products and Processes continues the OECD's review of environmental applications of biotechnology. It began with *Biotechnology for a Clean Environment* (OECD, 1994), which focused on bioremediation of polluted air, soil and water, and was followed by workshops in Tokyo in 1994, Amsterdam in 1995, and Mexico in 1996 (OECD, 1995, 1996, 1997).

Chapter 1, "**Industrial Sustainability and the Role of Biotechnology**", highlights the paradigm shift that has taken place since the early 1990s: the emphasis is no longer on the removal of pollutants from an already damaged environment, but on the need to reshape industrial process technologies to prevent pollution at the source. However, the concept of "clean technology" has appeared so quickly that the conceptual agenda is, in many instances, in advance of the necessary R&D, and also does not take account of the existing technological potential. Achieving "clean technology" or "industrial sustainability" – the two terms are largely congruent – will not be possible without a steady stream of creative innovations based on advanced science and technologies, among which biotechnology is likely to play an increasing role. Gaps between the conceptual agenda, R&D needs and technical possibilities can be narrowed by alerting governments, industry and the public to biotechnology's growing potential, but also to the bottlenecks which still must be removed to bring this potential to fruition.

Although definitions of sustainable development have frequently proved elusive, it is clear that any move towards industrial sustainability (lower relative consumption of energy and raw materials, reduction or elimination of waste) will affect all stages of a product's or process's life cycle. It will require new design principles based on a global and holistic approach to reducing environmental impacts: global because these impacts transcend national borders, holistic because short-term, piecemeal solutions to address a succession of issues in isolation will be less and less effective. One important means of integrating environmental issues into industrial design and operations is the adoption of Life Cycle Assessment (Chapter 4), which is the best, because holistic, approach to measure cleanliness. The LCA approach must always consider the "boundaries", that is, the points in a multi-step process at which an LCA is to begin and to end.

There are three main drivers of clean technology: economic competitiveness, with companies considering the advantages of clean products and processes in terms of market niches or cost advantages; government policies, which enforce or encourage changes in manufacturing practices; and public pressure, which takes on strategic importance as companies seek to establish environmental legitimacy.

The question of why adoption of clean technology has not been more widespread must be raised. One of the main contributions biotechnology could make is the controlled and rapid production of biological catalysts, including living organisms or their catalytically active constituents. These offer cleaner products and processes because they are more specific (fewer by-products) and more selective (need for less purified feedstocks) than their non-biological competitors; in addition, they are self-propagating. However, the perception of biotechnology as inherently cleaner is somewhat simplistic; biotechnology is not clean *per se*, just as chemical technology is not dirty *per se*. There are increasing examples of clean chemistry, and cost reductions derived from waste minimisation by chemical companies can be documented.

It is possible to foresee a growing role for industrial process biotechnology, both because it may afford clear economic and environmental benefits, and because the power of the tool itself continues to grow. The expectations of greater cleanliness come from the observation that living systems manage their chemistry rather more efficiently than man-made chemical plants, and that their wastes tend to be recyclable and biodegradable. This, along with our increasing ability to manipulate biological materials and processes, strongly points to a significant impact on the future of manufacturing industries.

Chapter 2, "**Current Industrial Applications of Biotechnology**", substantiates some of these findings. This industrial "state-of-the-art" chapter pulls together an overall picture of how modern process biotechnology is penetrating industrial operations. It describes processes that have reached at least pilot plant stage, and attempts to evaluate the economic importance of biotechnological applications to various industrial sectors. The six sectors examined are responsible for a large share of the industrially generated pollution in OECD countries: chemicals, pulp and paper, textiles and leather, food and feed processing, metals and minerals, and energy.

Biotechnology embraces a wide range of techniques, and none of these will apply across all industrial sectors. Nonetheless, the technology is so versatile that many industries that have not used biological sciences in the past are now exploring the possibility of doing so. Already, the economic competitiveness of a variety of biotechnological applications to achieve cleanliness has been established. This is essential, as environmental benefits alone have seldom driven the adoption of biotechnology-based processes. Such processes have been successfully integrated into some large-scale operations. However, a number of problems remain for industrial applications, particularly the entrenched infrastructure of companies that have traditionally relied on physical and chemical technology alone and whose engineers have no training in life sciences or technologies. Also, when the economic advantage of biotechnology-based processes over existing methods is not enormous, *e.g.* in the chemicals sector, the penetration rate of biotechnology is usually slow.

The chemicals sub-chapter reviews commodity chemicals, fine chemicals, enzymes, pharmaceuticals and crop protection chemicals. Chemicals manufacturing is a major generator of materials, a major consumer of energy and non-renewable resources, and a major contributor to waste and pollution. In these sub-sectors, market penetration of biotechnology varies. It is in the fine chemical industries that the impact of clean biotechnology is most visible.

While fossil carbon (oil, coal) is the single most important raw material for energy generation and for chemicals, the concomitant CO_2 emissions are a source of increasing concern because CO_2 is a major greenhouse gas. Biotechnology can contribute to reducing fossil carbon consumption and hence global warming in various ways: improving industrial processes and energy efficiency, and producing biomass-based materials and clean fuels.

In pulp and paper, market penetration of biotechnology used for clean production is particularly high in Europe, and biotechnology is becoming more important in the manufacture of textiles and leather throughout the OECD area. In the food and feed sector, the impact of biotechnology on clean industrial processes seems to be greatest in the United States. Biotechnology for mining and metals recovery covers two major technologies: bioleaching/minerals biooxidation, where superior cleanliness and economic profitability have been claimed in specific cases, and metals bioremediation and recovery.

In the energy sector, biotechnology has had a major effect both on economics and on environmental impacts. It has improved the overall efficiency of processes, particularly in the area of pollution control. Processes currently under development, such as biodiesel, bioethanol and biodesulphurisation, seek to replace energy-intensive and polluting systems with systems that are more environmentally friendly. The effect of rDNA methods on these technologies will be great, but large-scale application of rDNA has only recently begun and has not yet had dramatic effects.

Although the potential of biotechnology to reduce raw materials and energy consumption as well as wastes is attractive, there is a need for further encouragement, notably by government, particularly when the economic advantages are not overwhelming in the early stages of adoption.

Following the description of the current state of penetration of clean biotechnology, "**Science and Technology Trends and Potential**" (Chapter 3) attempts to look into the future, identifying major scientific and technological bottlenecks, needs and opportunities.

The first task is to identify "bottlenecks and unmet market needs" and their implications for future R&D. Technical issues affect the wider application of clean biotechnology, but potential scientific developments and solutions exist in each of the six industrial sectors. In a climate generally dominated by molecular biology, the neglect of bioprocess engineering and the related R&D is a particular danger: the future success of biotechnology relies crucially on improved biochemical engineering.

At the same time, large new opportunities are opening up: many current products and processes are regarded as environmentally unfriendly, and there is interest in novel substances that will minimise environmental and health risks. Thus, strategies to incorporate "green design principles" ("design for environment") into production processes are being encouraged.

The key area of opportunity is improved and novel biocatalysis (see Chapter 1). As less than 1 per cent of the micro-organisms in nature have been cultured, the search is on to examine the remaining, unexplored microbial biodiversity which presumably holds a great wealth of biocatalytic potential. However, the search for novel bioactive compounds, biocatalysts, and biomaterials in nature is only a part of this trend. Proteins and enzymes with novel functions and properties can also be obtained by improving upon currently known natural proteins or enzymes; the latter approach may even be more suitable for creating properties unlikely to have appeared in natural evolutionary processes. The current impetus for researching extremophiles (micro-organisms that live in extreme conditions of temperature, salinity, acidity, etc.) is the expectation that their enzymes will have improved catalytic performance in industrial conditions. Another, related advance is "directed evolution" of enzymes, a practical approach for tailoring enzymes for a wide range of applications.

Looking at the main areas of progress in the life sciences in general, four have particular strategic relevance for clean products and processes: bioconsortia and rDNA technology (which are methods for combining genetic potentials), metabolic pathway engineering, and bioinformatics. The merits of using bioconsortia (several strains of micro-organisms operating together) in industry are known, but progress has been difficult. A resurgence of interest in bioconsortia is accompanied by important discoveries, *e.g.* that bacteria, like ants, appear to be social organisms which send signals that can be studied. Recombinant DNA technology provides an even more powerful method for combining diverse genetic capabilities, thus permitting the engineering of organisms with new specific catalytic capabilities. Many biotechnological applications for cleaner industrial products and processes will rely upon recombinant micro-organisms. Most of the processes will be contained and hence subject to existing guidelines for industrial applications of rDNA (*e.g.* GILSP – Good industrial large-scale practices).

A new strategy now attracting much interest is metabolic pathway engineering. This means assembling in one organism a metabolic sequence whose individual stages have been taken from two or more organisms. Finally, the interdisciplinary field of bioinformatics must be mentioned. Such is its growing power that biological research itself may be shifting from traditional observation-experiment to so-called "data-mining", where innovative experiments will be undertaken *in silico*, rather than *in vivo* or *in vitro*.

Industry, government and the public are the main stakeholders for the development of environmentally friendly products and processes. Demonstration projects will be vital for bridging the gap between laboratory research and industrial implementation; this will give governments a specific role in the technological pursuit of cleaner products and processes.

"**Evaluating the Cleanliness of Biotechnological Industrial Products and Processes**" (Chapter 4) is a crucial issue. Everyone agrees that products and processes should be clean, but what is "clean", and how does one measure it? So far, limited experimental results and general scientific knowledge have argued for the cleanliness of biotechnological process technologies, in addition to their economic advantages. More rigorous proof would be desirable.

Several tools exist for evaluating the influence of technical products and processes on the environment. Life Cycle Assessment (LCA) evaluates potential environmental impacts of products or services over their entire life cycle ("cradle to grave"), taking a global and holistic approach, independent of the place and time when a product is made, used or disposed of.

This is currently the method of choice for assessing the cleanliness of industrial processes. It is also a particularly relevant method for determining how much biotechnology can increase cleanliness. LCA is confined to the material and energy balances of an activity; socio-political and economic criteria, which are also important for decision makers, do not fall within its scope.

LCA consists of four steps: definition of aims and scope, inventory analysis (collection of the relevant inputs and outputs), impact assessment (including "weighting", which is the most disputed aspect of LCA because it requires judging the relative importance of different factors, *e.g.* CO_2 emissions versus mercury pollution of soil), and fourth, interpretation. There is a high degree of consensus on the methodological framework, although the task of collecting the data can be very onerous.

LCA was first developed more than 20 years ago, but has until recently been little used for bioprocesses and products, partly because biotechnology has arrived relatively late on the scene and partly because it raises particular methodological difficulties. Also, many LCAs carried out in industry remain confidential. Nevertheless, six specific LCA examples comparing biotechnological with other processes are given from different industries. In all cases, LCA appears to confirm the superior cleanliness and economics of biotechnological operations. However, the sample is too small to allow for generalisations. Further methodological research is needed to improve LCA in general, and to extend it to biotechnology in particular.

"**Public Attitudes and Education**" (Chapter 5) reviews an issue which has already been mentioned as decisive for the final adoption of industrial biotechnology. Biotechnology can be seen as working in harmony, rather than in conflict, with the natural world, and the concept of clean technology based on biological approaches may therefore attract public support.

There is little specific quantitative evidence on public perceptions of biotechnology applied to cleaner industrial processes. Countries show wide differences in public awareness of and attitudes towards biotechnology in general (or specific tools and applications), and attitudes change over time. Some surveys (*e.g.* the Eurobarometer) can be read as encouraging for biotechnology, although it would be misleading to draw over-optimistic or far-reaching conclusions.

Of the six industrial sectors reviewed (Chapter 2), the food sector could raise problems in terms of public acceptance of food manufactured with clean, rDNA-derived biotechnologies. Consumer information (*e.g.* food labelling) is a significant issue of concern to the public that remains to be resolved.

Active measures need to be taken to promote a wider understanding of biotechnology as a basis of clean processes, and to accelerate a shift in outlook.

There is no universally appropriate strategy for promoting wider comprehension of a topic as complex as biotechnology, but there are some simple yet general messages that could be conveyed, *e.g.* that microbes play many positive roles in the natural world, although the public still sees them overwhelmingly as agents of disease. The target audiences include opinion leaders and editors, particularly in the media (newspapers, radio, television), pupils and their teachers at all school levels, science and engineering students, non-technical industrial staff, and politicians at local, national and supranational levels. Schools have been shown to be highly receptive communities within which to develop greater understanding of sustainability, clean processes, biotechnology, etc.

In the higher education sector, the main need is to broaden the training of biotechnologists and engineers and to integrate LCA, sustainability and other relevant concepts into curricula and hence future views. Similar shifts in perspective are required in the education of non-scientific industrial staff (retraining). Finally, there is a clear need to enhance the scientific awareness of government regulators and their constituencies on issues of biotechnology for clean industrial products and processes.

"**National and International Policies**" are discussed in Chapter 6. Although these are recognised as a major driving force – often the single most important – it was possible to undertake only a brief review, based on three countries (Canada, Germany, Japan). One of the most visible marks of policies for cleaner technology is their roots in international commitments (*e.g.* the Rio Declaration on Environment and Development of 1992), which explains certain national similarities. However, not all national policies in this area have their origin in international developments.

The number of policy and legal initiatives that encourage cleaner technology and are implicitly relevant to clean biotechnology is large and increasing. Some have led to new products, increased industrial efficiency, and new jobs; others have been seen as too inhibitory. Because the policy framework for cleaner industrial products and processes can have both positive and negative effects, both need to be considered. However, there seems to be no national or international legislation that explicitly identifies biotechnology as a preferred tool for cleaner products and processes, even if some countries consider it as a critical "enabling technology".

Policies which involve the general public, by modifying consumer preferences and lifestyles, will, in the long term, have the most far-reaching effects.

The last chapter, "**Conclusions and Policy Implications**", summarises the main findings of the report, and draws policy implications for the main "stakeholders", particularly government and industry which must act together to facilitate the penetration of biotechnology as an enabling technology. R&D policy will be critical, particularly in building a bridge from basic research to final implementation. This can be done by joint government-industry support for demonstration projects that show biotechnology's applicability.

The following ten points contain the main messages of the final chapter:

- **Global environmental concerns will drive increased emphasis on clean industrial products and processes.**
- **Biotechnology is a powerful enabling technology for achieving clean industrial products and processes that can provide a basis for industrial sustainability.**
- **Measuring the cleanliness of an industrial product or process is essential but complex; Life Cycle Assessment (LCA) is the best current tool for making this determination.**
- **The main drivers for industrial biotechnological processes are economic (market forces), government policy, and science and technology.**
- **Achieving greater penetration of biotechnology for clean environmental purposes will require joint R&D efforts by government and industry.**
- **For biotechnology to reach its full potential as a basis for clean industrial products and processes, beyond its current applications, additional R&D efforts will be needed.**
- **Because biotechnology, including recombinant DNA technology and its applications, has become increasingly important as a tool for creating value-added products and for developing biocatalysts, there is a strong need for harmonised and responsive regulations and guidelines.**
- **Market forces can provide very powerful incentives for achieving environmental cleanliness objectives.**
- **Government policies to enhance cleanliness of industrial products and processes can be the single most decisive factor in the development and industrial use of clean biotechnological processes.**
- **Communication and education will be necessary to gain penetration of biotechnology for clean products and processes into various industrial sectors.**

PREFACE

This report examines biotechnology as a means of achieving clean or cleaner industrial products and processes. It compares biotechnological processes with competing means of securing similar goals.

Clean technology

All stages of the life cycle of a product or process may adversely affect the environment by using up limited resources of materials and energy or by creating waste. Any substitution or change that reduces consumption of materials and energy and production of waste – including, for example, recycling of materials and energy – may be regarded as more environmentally friendly or ‘‘clean’’. Clean technology may also be equated with reduced risk. Life Cycle Assessment is one way of comparing the relative cleanliness of a product or process.

Chapter 1 reviews the potential role of biotechnology in clean industrial processes and sets the stage for viewing clean processes in the context of industrial sustainability. Chapter 2 discusses: *i)* the main industrial sectors for which biotechnological methods appear appropriate and timely; *ii)* the extent to which biotechnological thinking and practice are being introduced into industrial sectors that have serious environmental impacts; and *iii)* the economic competitiveness of biotechnology for clean products and processes in these sectors. It gives examples of industrial biotechnology applications, organised by industrial sector, and discusses their economic impact. Chapter 3 examines scientific and technological innovations across the range of biotechnologies and the opportunities for their adoption, as well as R&D priorities. It presents the technological drivers and the additional R&D needed to introduce biotechnology for clean industrial processes and products. Chapter 4 describes life cycle concepts and the tools available or requiring development in order to make quantitative assessments of what constitutes ‘‘clean’’ or ‘‘cleaner’’ when evaluating the merits of new or alternative technologies, products or processes. Life Cycle Assessment provides a systematic means of prioritising R&D initiatives aimed at clean industrial practices. Chapters 5 and 6 consider the role played by the general public and government in the implementation of clean technology in industry. They discuss legal and policy frameworks, public perception of biotechnology, and the need for information exchange, education and training. Chapter 7 draws conclusions and makes recommendations regarding industrial and government policies that can affect how biotechnology is used by industry to contribute to cleanliness and sustainability.

INDUSTRIAL SUSTAINABILITY AND THE ROLE OF BIOTECHNOLOGY*

- **Industrial sustainability demands a global vision and co-ordinated policy approaches.**
- **In an industrial context, sustainability is equated with clean industrial products and processes.**
- **Biotechnology is competitive with and in many cases complements chemical methods for achieving clean technologies.**
- **It is essential to determine what is clean or cleaner, using Life Cycle Assessment and related methods.**
- **Biotechnology is a versatile enabling technology that provides powerful routes to clean industrial products and processes and is expected to play a growing role.**

INTRODUCTION

In the first OECD report on biotechnology (Bull *et al.*, 1982), issues of environmental concern were little in evidence. At that time, the emphasis placed on waste management revealed an implicit acceptance of a waste-generating economy, and biotechnological options were considered either for waste treatment, or to a much lesser extent, for use as a feedstock. The intervening years have seen many developments and commercial applications in end-of-pipe, disposal and remediation biotechnology (OECD, 1994; 1995*a;* 1996; 1997) and the gradual emergence of technologies directed towards waste minimisation or prevention. Recycling of materials, minimisation of energy utilisation, retrofitting of existing industrial processes to alleviate pollution, and applications of innovative science have provided routes to clean or cleaner technology. Therefore, this report, which promotes biotechnological methodologies for clean industrial products and processes, represents a logical approach to sustainable development.

Box 1.1. **Biotechnology**

The definition of biotechnology used in this report is "the application of biological organisms, systems and processes to the production of goods and services". By drawing a line at the time in the late 1950s and early 1960s when the structure and function of nucleic acids were being discovered, it is possible to distinguish between the earlier, traditional biotechnology of bread and wine making, for example, and second generation biotechnology which, in part, makes use of recombinant DNA technology. It must be stressed, however, that biotechnology is wider than genetic engineering and draws heavily upon process technology, chemistry and classical engineering.

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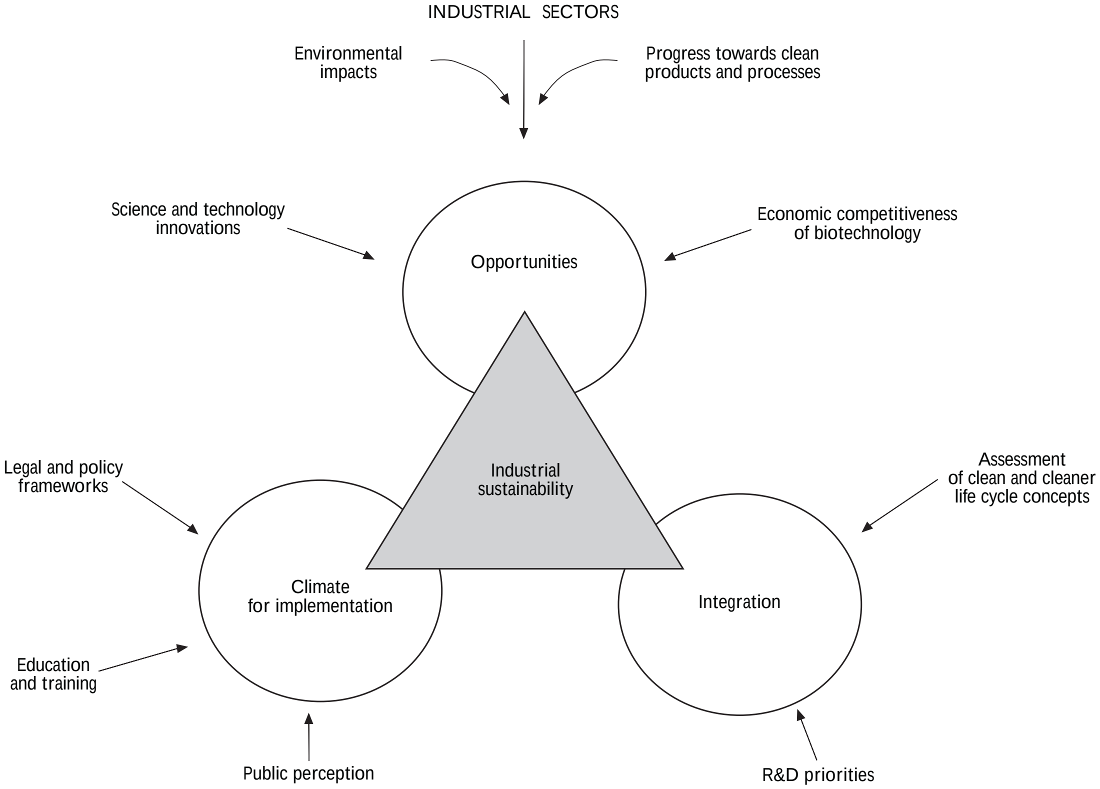
* This chapter was drafted under the responsibility of Dr. A. Bull, University of Kent (UK).

The report fits well into the changing framework of the OECD's overall programme of work, which gives high priority to environmental sustainability. The 1997 publication, *Sustainable Development: OECD Policy Approaches for the 21st Century*, testifies to the broad range of relevant OECD work in this area, and also, to quote the OECD's Secretary-General, to the Organisation's ''growing awareness that economic growth can no longer be credibly pursued without a much stronger concern for its sustainability''. Sustainable development will be impossible without a steady stream of creative innovations based on advanced sciences and technologies, among which biotechnology may well play an increasing role. The report focuses on the science and technology aspects and the potential contribution of biotechnology to clean industrial processes and products (Figure 1.1).

◆ Figure 1.1. ***Analysing existing and potential contributions of biotechnology to achieving industrial sustainability***



Source: Author.

Clean technology represents a new paradigm, or at least a move in that direction. This concept has appeared so quickly that the conceptual agenda is, in many instances, in advance of the necessary R&D. A primary objective of the report, therefore, is to indicate the technical bottlenecks, and the scientific advances, that affect the extent and pace of biotechnological input into cleaner products and processes. Box 1.2 gives a selection of very recent inventions and discoveries that represent possibilities for near- and longer-term exploitation, which in every case can be expected to advance clean technology and industrial sustainability.

Box 1.2. **Biotechnology potential: Some recent examples**

Pulpwood trees

- The world demand for cellulose fibres is enormous, 64 million tonnes in the United States alone.
- Pulp production requires removal of lignin from the wood, a process that is expensive in terms of energy and chemicals, and environmentally unsustainable in terms of the huge production of pulp mill effluent.
- Conifer wood requires more intensive pulping conditions than hardwood lignin but the quality of its cellulose fibres is superior.
- Genetic manipulation of lignin genes now opens up the prospect of reducing lignin content and modifying lignin chemistry in conifers, thereby enabling cleaner pulping.

Stabilised enzymes

- Operational stability is an on-going requirement for industrial biocatalysts.
- The development of cross-linked enzyme crystals (CLECs) is one means of achieving stability.
- CLECs are zeolite-like lattice structures that impart stability to the catalytic site under a wide range of reaction conditions.

Biochemical signals

- Plants, including major crops such as maize and cotton, release volatile signalling chemicals when attacked by insect pests.
- These chemicals act as attractants of other, parasitic insects.
- When the beet armyworm caterpillar feeds on maize, the plant releases a mixture of chemicals that attracts a parasitic wasp to the scene.
- The wasp lays its eggs in the caterpillar which is ultimately digested by the emerging wasp larvae.
- Biochemical understanding of such insect-plant interactions may lead to novel developments in environmentally friendly pest control.

Source: Podila and Karnosky, 1996; Anon., 1997.

In light of the need for industrial sustainability and clean technology, this report aims primarily:

- to alert government policy makers to the enormous potential of these new technologies;
- to alert industry to new technology opportunities that are compatible with clean processing;
- to encourage greater public understanding of the growing number of low-risk technological options;
- to provide technical information and orientation relating to the state of the art, as an aid to policy formulation;
- to provide a road map for R&D leading to increased penetration of biotechnology and the implementation of cleaner industrial practices.

The report highlights the need to integrate science, economics, legislation and education in order to ensure the successful penetration of sustainability thought and practice into industrial activities at all levels. The position of small and medium-sized industrial enterprises is a significant one in this context. In the United States and in Europe, over 99 per cent of all companies fall into this category (less than 500 employees) and in Europe 93 per cent are so-called micro-enterprises (less than ten employees) (Geiser and Crul, 1996). This report is intended to go some way towards increasing the knowledge of biotechnology and of the science of environmental problems, both in companies and among the public.

SUSTAINABILITY: DEFINITION AND GOALS

Box 1.3. **Sustainability**

Definitions of sustainability and sustainable development have frequently proved to be elusive. This report follows the lead of the World Commission on Environmental and Development (Brundtland, 1987):

Sustainable development: strategies and actions that have the objective of meeting the needs and aspirations of the present without compromising the ability to meet those of the future.

Human activities – industrialisation, urbanisation, agriculture, fishing, forestry and mineral extraction – have profound impacts on the world's environment and the sustainability of environmental quality. There is growing appreciation that nationally, regionally and globally, resource management needs to be improved and the amounts of wastes and pollution generated need to be reduced. Indeed, all signatories to the Rio Declaration on Sustainable Development (see Box 6.1 in Chapter 6) are called upon to reduce, and if possible to eliminate, unsustainable patterns of production and consumption. The Brundtland concept of sustainability, as developed by Hall and Roome (1996), makes the following additional assumptions:

– sustainable development provides a framework for integrating environmental policies and development strategies;

– sustainable development will make an increasing contribution to the future shaping of global technological, socio-economic, political and cultural change and will define the boundaries of what is possible and what is desirable;

– while no single blueprint for sustainable development is likely to be agreed, sustainability should be regarded as a global imperative.

Sustainable development is guided by the need for: *i)* better balance between conventional ideas of economic growth and the maintenance of environmental resources; *ii)* improved intragenerational and intergenerational equity in economic and environmental terms; and *iii)* ensuring sustainability in ways that have both local and global relevance. The difficulty with these definitions and statements is that they are general and lack operational guidance for practitioners and policy makers. Consequently, we need to address such questions as: Which current activities are consistent with sustainable development? What policies are required to achieve sustainable development? What actually are we aiming to sustain? The last of these might be interpreted in terms of a service, an industry, or the planet's very life support systems.

Sustainable industrial development means continuous innovation, improvement, and use of ''clean'' technologies to make a fundamental change in pollution levels and resource consumption. New approaches are needed to manage increasing industrialisation and urbanisation world-wide in a sustainable way. Because all stages of a product's or process's life cycle may affect the environment, design principles based on a holistic approach to novel processes, which consider all aspects, from choice and quantities of raw materials to improvement of recovery during waste management, can be employed to reduce environmental impacts. An environmentally friendly process would, in principle, have: *a)* low consumption of energy and non-renewable raw materials (especially fossil fuel feedstocks) relative to the products or services delivered; and *b)* reduction or elimination of waste (including materials and energy recycling and energy use). Thus, the primary objective of any strategy designed to achieve such a process would be to maximise both *a)* and *b),* from raw materials through production to consumption and ultimate disposal of products. Biotechnology can make a significant contribution to achieving these goals.

Globalisation

A discussion of industrial sustainability is incomplete without reference to globalisation and to developing countries – issues which are extensively discussed both within and outside the OECD. In the absence of a more comprehensive examination of these crucial issues, which was not within the remit of this report, a few remarks must suffice.

The move towards globalisation of the world economy and the internationalisation of production are leading to a shift of economic focus from national to global level. It will be important, therefore, to monitor the relationship between globalisation and sustainable development. Are they working in concert or in opposition? For example, clean production and more efficient patterns of consumption introduce prospects of depressed demand for exports of raw materials and agricultural commodities, and a raising of green protectionist trade barriers as a result of more exacting requirements from manufacturers, retailers and consumers. This could cause trade problems, particularly for exports from developing countries. In the chemicals sector, for example, the practice of positive supplier vetting and vendor assessment has existed for several years, and companies increasingly make detailed environmental or even full life cycle audits prior to placing orders. Here, market forces, not regulations, are driving the scale and pace of change.

In addition to the question of international trade, the issue of industrial sustainability is also concerned with industrial delocalisation, environmental management strategies of multinational companies, and the attitudes of industries and governments in industrialising countries towards the environment. It has been argued that multinational companies have shifted their polluting and hazardous manufacturing operations to countries where environmental regulations and their enforcement are less rigorous. A World Bank investigation (Low, 1992) concluded that whereas "national differences in environmental regulations have not been a major explanatory factor in changing international patterns of location of dirty industries", "dirty industries have expanded faster in developing countries than the average rate for all industries over the last two decades, and faster than in industrial countries". The transfer of clean or cleaner technology may be advocated as the remedy in such cases. However, the problem is then shifted to the capacity of such countries to assimilate major technological and social change. Thus, the lack of a critical mass of human and other resources in small developing countries may deprive them of the new opportunities for sustainable industrial development.

TOWARDS INDUSTRIAL SUSTAINABILITY

The ecosystem concept was developed earlier in this century to define interactions which occur between living organisms and the physico-chemical environment. Moreover, ecosystems are not isolated systems but are linked both at local and regional scales, so that environmental insult at the local scale may result in global perturbations. The significance of this global connectivity has only recently been fully recognised: "... the late 20th century marks a critical turning point in the ecological history of human civilisation. For the first time ... the aggregate scale of human activity is capable of altering global biophysical systems and processes in ways that jeopardize both global ecological stability and geopolitical security" (Rees, 1997). Consequently, the implications for sustainability force attention towards humans as the dominant consumers in all of the world's ecosystems.

In the past, treatment technology of industrial wastes was promoted at the expense of investment in the long-term strategies needed to bring about waste minimisation; management policies focused on treatment and disposal rather than on waste reduction and recycling. The development of a sustainable industrial economy demands a global and holistic perspective: global because certain problems are encountered in all countries (*e.g.* environmentally hazardous chemicals, dissipative pollution) or transcend national boundaries (*e.g.* transboundary pollution, climate change); holistic in that environmental problems require systematic analysis, discovery of solutions, and prioritisation of actions rather than narrowly conceived, short-term, piecemeal steps.

The concept of industrial sustainability is founded on an analogy between natural ecosystems and industrial systems, which considers them as part of a totality that encompasses all their interactions with the environment and with each other and is a means of achieving both industrial and overall sustainability. Various models of industrial sustainability have been formulated (see Annex 1.1). These models provide a basis for improving the efficiency of industrial processes and hence their cleanliness and sustainability.

A comprehensive realisation of industrial sustainability is probably very difficult, and the introduction of even quasi-industrial ecosystems is a long way into the future. Nevertheless, a number of commercial operations have already adopted these principles. At present, they are mainly in the heavy industrial sectors or sectors where environmentally hazardous processes have been documented (Kirkwood and Longley, 1995). The challenge for biotechnology is to provide the impetus and appropriate tools for wider penetration of the industrial sustainability concept. Short-term, piecemeal solutions are no longer acceptable for dealing with environmental problems. "The difficulty with this fragmented approach is that it addresses a succession of new issues without necessarily resolving the previous one[s], thereby creating the impression that [they] no longer matter[s]. Attention focuses on one subject, overshadowing others which are no less important. This approach also fails to treat the environment as a single system, which makes it virtually impossible to show people how their behaviour affects the environment" (Dutch Ministry of Housing and Environment, quoted by Johnson, 1997). The single most important outcome of accepting environmental issues into industrial design and operations is the adoption of Life Cycle Assessment (LCA), which is introduced below and treated in detail in Chapter 4.

Box 1.4. **Biotechnology and process energy saving**

The search is on for extremozymes that are robust and operate at high temperatures. These enzymes nevertheless operate at temperatures well below those of conventional petrochemical processes, and the more extreme conditions of the latter, together with their more exotic construction materials and greater proportions of by-products (wastes), might be expected to translate into higher energy consumption per unit of product. However, the extra energy cost of working with high temperature thermochemistry on petrochemical feedstocks is generally more than offset by the energy cost of removing water from biotechnology product streams. The energy consumption advantages or disadvantages will only be resolved by making a detailed LCA to compare all these factors.

WHAT IS CLEAN TECHNOLOGY?

Our concept of clean technology is based on, but is more comprehensive than, the UNEP definition of clean production (Clift and Longley, 1995):

> *Clean technology: a conceptual and procedural approach to industrial activities that demands that all phases of the life cycle of a product or of a process should be addressed with the objective of prevention or minimisation of short- and long-term risks to human health and to the environment.*

The essential feature of clean technology is avoidance of environmental damage at the source. Cleaner technologies move in this direction. The use of the term "cleaner" has been criticised by some commentators as a compromising, gradualist position that deflects attention away from truly eco-compatible development. However, under present conditions, it represents an attainable, pragmatic goal and has been adopted by the OECD (1995*b*):

> *... technologies that extract and use natural resources as efficiently as possible in all stages of their lives; that generate products with reduced or no potentially harmful components; that minimise releases to air, water and soil during fabrication and use of the product; that produce durable products which can be recovered or recycled as far as possible; and are energy-efficient.*

While such concepts may lack definitional clarity, this should not be seen as a weakness; what is essential is that they stimulate new thinking in order to encourage clean technological innovation. Clean technology will mean a profound shift in our view of the planet, towards actions that are integrated and global in scope and sustainable in their effects. The objectives of clean technology can be regarded as coincident with those of industrial sustainability.

As Green and Irwin (1996) and others have pointed out, the technical literature portrays an optimistic view of the economic benefits of clean technologies (savings on feedstocks, water and energy; reduced costs of pollution treatment; new products and processes leading to new market opportunities; stimulation of technological innovation). So why has the adoption of clean technologies not been greater? Several opinions have been offered: end-of-pipe treatments remain as cheaper options; regulatory authorities' continued preoccupation with the symptoms rather than the causes of pollution; perceived length of payback period for return on investment; need to amortise existing plant; lack of information; cost-effectiveness not established (*e.g.* problems of marketing new products and processes); and the degree of availability of acceptable clean technology. But significant progress has been made in the recognition and implementation of clean technology ideas, as Table 1.1 shows.

Table 1.1. **Progress towards corporate environmental actions**

	Trends	Companies
1.	Fundamental rethinking on disposability, risk, responsibility, right to pollute	3M, Monsanto, Dow Chemical
2.	Increased adoption of environmental policies and involvement of industry associations	Monsanto, Dow, ICI, Westinghouse, Chevron, 3M, McDonald's, Bell Canada, Responsible Care, International Chamber of Commerce, Keidanren, Baum, S.C. Johnson
3.	Spread of holistic full-cost and impact analysis; Life Cycle Assessment; total environmental audit	AT&T, Proctor and Gamble, Esprit, Smith & Hawken, The Body Shop, Patagonia, Ben & Jerry's
4.	Industrial ecology experiments	Novo Nordisk, Kemira, Statoil, Asnaes (Kalundborg)
5.	Collaboration between companies and environmental organisations	Fuji Photo Film and Audubon Safeway and Earth Island Inst., McDonald's and Environmental Defense Fund, Merck and Nat. Inst. of Biodiversity of Costa Rica, New England Electric Utilities and National Defense Council and Conservation Law Foundation
6.	Growing board involvement in corporate stewardship	DuPont, Novartis, ICI, Monsanto, Henkel, Ferris Industries
7.	Greater environmental accountability forced by accidents	Union Carbide, Exxon, Sandoz
8.	Increased actual/potential legal liability for environmental damage caused by accidents	Union Carbide, Exxon, Shell, General Electric, Allied Signal

Source: Fischer and Schot, 1993.

Drivers of clean technology

Clean technologies are in most cases specific to a given process and even to a type of process within a single company. Because the design and development of clean technologies are most often carried out within companies, it is difficult to assess their overall economic impact for an industrial sector. Clean technologies may replace environmental (*e.g.* end-of-pipe) technologies or be adopted when new production processes reduce costs in comparison to the previous production system. They may also result in better process performance or product quality. Investments in clean technologies are usually made to improve product quality and process economics and to comply with environmental legislation. The implementation of clean technologies by industry is driven by several factors, particularly economic competitiveness, government policies, and public interest.

Economic competitiveness

Companies consider the advantages of clean products and processes in terms of market niches and/or cost differentiation. Moreover, depending upon their place in the market and their technological innovation, companies will make strategic choices about developing clean technology for offensive or defensive reasons. It may not be easy to determine some of the economic benefits deriving from the adoption of clean processing, because it is difficult, for example, to weigh the costs of adoption against the probability of risk, *e.g.* avoidance of litigation costs where hazardous materials or practices are involved. Estimates of expenditure on clean technology in the 1990s are put at £140 billion ($240 billion) for the United Kingdom alone, while spending in the European Union could exceed the current R&D expenditure of the European chemicals industry (Clark, 1995). The opportunities for the introduction of new technology and for research directed at environment-compatible chemical processes are clear. In order to determine the economic contribution of biotechnological processes to cleaner production, the total market share of biotechnology companies for each sector is analysed in Chapter 2.

A distinction can be made between three categories of market contributions by biotechnology products:

- *Sales of new products directly attributable to the use of modern biotechnology*. This includes novel products modified by rDNA technology (*e.g.* genetically modified seeds or biopharmaceuticals), as well as products and processes that directly exploit the knowledge base of modern biotechnology (*e.g.* new environmental services and fine chemicals for pharmaceuticals).
- *Sales of products manufactured by improved processes that make direct use of modern biotechnology (direct impact)* (*e.g.* recombinant insulin). In this case, modern biotechnology is applied in the manufacturing process, but the end product is not modified. This category excludes products based on purchased processing aids (*e.g.* enzymes).
- *Sales of products manufactured by improved processes using the products of modern biotechnology from other industries (indirect or secondary impact).* This includes efficiency improvements in manufacturing processes through the acquisition of new processing aids (*e.g.* enzymes) and increases in the value of final products through the use of new ingredients.

Together, these three categories represent total biotechnology-related sales (BRS).

Government policies

Industry's strategy is to ensure that businesses operate within pre-agreed legal limits in order to minimise both liabilities and changes in operating practices. It has been argued that government policies can have a positive effect on a country's competitiveness and that the more stringent the policies, the greater the competitiveness in the long term (see OECD, 1994; Chapter 6 of the present report, with its annex; and Management Institute for Environment and Business, 1994, for case studies). In 1990, OECD Member countries invested approximately $100 billion in environmental protection, the great majority of it determined by the need to comply with environmental regulations.

Public interest

Pressure due to public awareness is a potent force for change over a broad spectrum of environmental issues and more than compliance may be required when companies' compliance does not appear to meet public expectations for "green" processes and products. Thus, establishing environmental legitimacy may take on strategic importance for industry. For many companies, environmental reporting has become a regular practice in response to shareholder demand and public expectations. "Green" products have increased market value.

MEETING THE GOALS OF INDUSTRIAL SUSTAINABILITY: BIOTECHNOLOGY IN CONTEXT

Industrial uses of biotechnology

The growth of our understanding of biological complexity, whether at the level of genetics, the organism, or the ecosystem, strongly underpins biotechnology. Biotechnology represents a wide-ranging set of tools, which can be used to improve large-scale fermentations to produce chemicals such as ethanol by living organisms, at one end of the spectrum, all the way to using minute parts of biological molecules as sensors in analytical devices at the other. It is important, therefore, to recognise that very few truisms apply across all applications, that no case study is appropriate for all industries, and that there is no irrefutable trend in all industrial sectors.

Industrial applications of modern biotechnology were for many years spin-offs of the investments made in medical biotechnology. Since the needs of industrial processes and product development were seldom directly served by the science and technology developed for the pharmaceutical industry, biotechnology has penetrated other industries more slowly. Indeed, industrial biotechnology has been such a backwater that, to Wall Street investors, "biotechnology" often means medical biotechnology. Nonetheless, biotechnology applications have made their way into many industrial sectors in recent years (see Chapter 2), and patterns of usage are beginning to emerge which suggest that the future economic impact of this technology will be significant.

Biotechnology enables the rapid and controlled production of biological catalysts, including living organisms or their catalytically active constituents. Biocatalysts are important both because they offer the industrial world cleaner processes and products and because they are more specific and more selective than their non-biological counterparts. This means that biocatalysts are capable of making fewer by-products (specificity), and can start with less purified feedstocks (selectivity). Furthermore, biocatalysts are self-propagating, so they can be used in low value-added applications such as waste treatment.

Although biocatalysts offer advantages, they also present a number of problems for industrial applications, and, until recently, these have often outweighed the advantages. Major problems have included the fragility of biocatalysts, the need for large amounts of water, low volumetric productivity, and the cost of the catalysts. Many of these problems have been addressed and overcome through new designs for bioreactors and catalyst improvement programmes. Indeed, a major advantage of biocatalysts is their amenability to continuous improvement. Yet, even as technical impediments are being overcome, the entrenched infrastructure in many industries continues to present a significant challenge for the widespread adoption of biotechnology by industries that have traditionally relied on physical and chemical technology.

Within any given industrial sector, areas where biotechnology has a potential impact can be traced along the value-added pathway from feedstocks, through processing and waste management, to product performance. For example, alternative feedstocks, especially renewable or sustainable feedstocks, are sometime more accessible via biotechnological than chemical routes. Pilot studies are under way, for instance, for producing succinic acid and polyols from agricultural resources rather than from the traditional petrochemical feedstocks. These processes use a combination of traditional chemistry and biotechnology to convert biological resources into chemical feedstocks. Biotechnological methods are also being employed to upgrade feedstocks in the energy sector, where biodesulphurisation of oil seems to be a viable "cleaner" alternative to chemical methods and is currently in pilot stage trials.

When feedstocks are changed, the products may change as well, sometimes dramatically so. In other cases, a biotechnological step can be introduced into a process in such a way as to retain the same feedstocks and products, while making the process more efficient. There are examples in sectors as diverse as chemicals, pulp and paper, food, and textiles.

New products from industrial biotechnology include more functional products, such as biodegradable polymers, optically active chemicals, and enzymes for use in detergents and feeds. Biocatalysts help make it possible to develop "smarter" products; these can offer more functionality for approximately the same cost as the products they replace.

In the context of this report it is important to recognise two things: *i)* the perception of biotechnology as an appropriate and clean technology, while well founded, is somewhat simplistic; *ii)* the multifaceted nature of biotechnology may make it difficult to assess its impact in different industrial sectors. In the case of the paper industry, for example:

- biotechnology will allow the breeding of superior pulp trees with lower or different lignins, altered fibre structure and higher yield, reflecting on paper quality and throughput;

– biopulping assists fibre release and enzymes improve water drainage when drying; this results in better paper quality (colour fastness, strength) and also lower energy consumption for a given throughput;

– biological deinking will replace mechanical deinking with an, as yet, unquantified energy saving;

– biobleaching is replacing the use of environmentally unfriendly chemicals;

– enzymatic biofilm removal reduces manufacturing down time and reduces costs;

– the above, plus biological water treatment, means that some paper mills now recycle 100 per cent of their water.

Thus, energy, environment, costs, quality, productivity and regulatory factors all may be identified as drivers of biotechnology innovations. As to which driver is the most important, the answer probably will depend on the particular industry: in the case of paper, industry response is based on achieving higher productivity and complying with increasingly stringent regulations.

Comparing the cleanliness of biotechnology with chemical technology, for example, is misleading and may even be counterproductive. Biotechnology *per se* is not necessarily clean, just as chemical technology is not invariably dirty. Valid comparisons of competing technologies or processes can be made only through carefully designed LCAs and the application of similar, objective, holistic criteria. That biotechnology has attributes that makes it eminently attractive for industrial sustainability is indisputable. The use of enzymes for biopulping reduces energy demand and the pollution load of wood pulping, and the use of biocatalysts to produce specific chemical intermediates for the synthesis of cleaner and safer industrial and pharmaceutical products are but two examples of the versatility of biotechnology in this context. An especially important benefit of biotechnology is the ability to produce substances that are chiral chemicals. Chemical processes usually produce racemic mixtures (but see Annex 1.2, Novel Clean Chemistry). Biocatalysis, in contrast, can produce enantiomerically pure chemicals, or can resolve racemic mixtures, so that complicated separation processes are avoided. The preparation of enantiomerically pure chemicals is crucial for the development of new drugs and pesticides, for example, where the inactive form of the chemical may be hazardous (*e.g.* thalidomide) in addition to being wasteful of raw materials.

Clean chemistry

The public's view of the chemical industry has often been a negative one, which is perpetuated by concerns about its unfavourable environmental record, the hazards associated with manufacture and transportation, and its generation of waste. In the chemicals industry, wastes are generated from feedstocks and/or impurities in the feedstocks, the reaction(s), auxiliary chemicals, separation and purification stages, and energy use. With respect to reactions, those that produce stoichiometric amounts of waste are problematic, unless the waste by-product can be used. By-products also can arise as a consequence of secondary reactions (*e.g.* chemical processes for acrylamide production that result in sulphates or acrylic acid). The financial impact of waste minimisation can be substantial (see Box 1.5).

Governments, research organisations, intergovernmental and non-governmental organisations, and the chemicals industry itself have all taken initiatives to promote clean products and processes. These include the OECD Pollution Prevention and Control Group, the UNEP industry sector working parties on cleaner production in pulp and paper, textiles, tanning, petrochemicals; the European Chemical Industry SUSTECH initiative for cleaner manufacture; and the Responsible Care initiative, which is aimed at improving all aspects of health, safety and environmental protection. In several countries, participation in this initiative is a condition of membership in professional chemical industry associations. In a number of OECD countries, basic research programmes have been set up to address issues such as catalysis, simpler synthetic processes, alternative routes to products, and the production of toxic intermediates *on demand.* Annex 1.2 contains illustrative examples of novel clean chemistry opportunities in the areas of catalysts, reaction media, support materials, and reaction enhancers.

Box 1.5. **Financial implications of waste minimisation**

Consider the cost benefit derived from waste minimisation measures (expressed under cost of sales) in a large pharmaceutical company and a small agrochemicals company. The top section of the table below defines the base-line cost of sales and profits while the bottom section shows the effect of a 5 per cent saving in cost of sales resulting from waste minimisation. The different manufacturing activities have different relative levels of costs for raw materials and consumables, and the increases in profit reflect the reduced cost-of-sales burdens. In every case, however, the point is obvious: a modest investment in waste minimisation can mean major cost benefits.

Financial benefits of waste minimisation in chemical production

Company	Sales ($ bn)	Cost of sales (%)	Profit[1] ($ bn)	Profit (% sales)	Profit increase (%)
Cost of sales and profit					
LP	7.477	23.7	1.1300	15.1	
SA	0.060	48.3	0.0035	5.9	
Effect of a 5% saving on cost of sales due to waste minimisation					
LP	7.477	22.5	1.2190	16.3	7.88
SA	0.060	46.0	0.0049	8.2	40.00

LP = large pharmaceutical; SA = small agrochemical.

1. Profit before interest and taxes.

Source: Braithwaite, 1995.

Determining the "cleanliness" of industrial processes

Life Cycle Assessment is a method for making comparative evaluations of entirely different technologies, for comparing an original process or activity and an improved version of that process, and for evaluating alternative products and processes. It is a basic tool for addressing the question, "How clean is the technology?" The adoption of life cycle concepts encourages companies to look systematically and holistically at products over their complete lifetime ("cradle to grave") rather than to focus only on the manufacturing stage. This type of analysis offers a way to:

- decide whether a process, product or service is in fact reducing the environmental load or merely transferring it upstream to resource suppliers or downstream to treatment or disposal;
- determine where in a process the most severe environmental impact is created;
- make quantitative comparisons of alternative process options and of competing technologies.

Box 1.6. **Life Cycle Assessment**

In 1993, Life Cycle Assessment (LCA) was defined by the Society of Environmental Toxicology and Chemistry (SETAC) as: "*... a process used to evaluate the environmental burdens associated with a product, process or activity by identifying and quantifying energy conversion, materials used, and waste released to the environment, to assess the impacts of those energy and materials uses and releases to the environment, and to identify and evaluate opportunities to obtain environmental developments.*"

Identification of ''key issues'' is an important step in improving the reliability of LCAs. In one sense, ''key issues'' relate to prioritising R&D for product and process improvements which promise the greatest environmental gain. The term is also being used to define research into the reliability of LCA, particularly as it relates to inventory, *i.e.* the application of life cycle screening to improving the reliability of assessment.

Various organisations have developed management instruments for achieving improved environmental performance. For example, the European Commission's Eco-Management and Audit Scheme (EMAS) was introduced as a voluntary means of environmental auditing, with the intention of providing an internal management tool for monitoring performance and an external performance indicator. EMAS emphasises such issues as eco-efficiency and cleaner production, without seriously questioning life cycles or indirect social and environmental effects. Although EMAS was only launched in 1995, it is being argued that it should be replaced by an LCA approach and a move towards ISO-type standardisation.

LCA boundaries

While Chapter 4 treats Life Cycle Assessment in more detail, it is worth emphasising one other point on the subject: boundaries for analyses. There are two aspects to the definition of boundaries for LCA. First, what are the boundaries of LCA *per se;* second, to what extent should LCA include economic and/or risk components. In some cases, not all stages of the life cycle may be included; for example, the waste management stage may be omitted if the intention is to assess materials from the cradle to the factory gate. Downstream, what weightings might be given to wastes and products that are economically and technically amenable to recycling, to those that are not economically but are technically amenable to recycling, and to those that are not amenable to recycling and result in dissipative loss? In current industrial activities, many materials fall into the final category.

Box 1.7. **LCA boundaries**

The beginning and endpoints in the multi-step LCA process are called the LCA boundaries. Their position is a matter of choice when making an analysis and may be determined by any number of external factors. This is especially true for biological processes such as biofuel production, where it is relevant to ask which activities and processes should be considered part of the production system and which part of the wider environment? When considered as part of the production system, sunlight, soil fertility, CO_2, H_2O, etc., are inputs, but when these are considered as part of the environment, biomass is the input.

Questions also arise as to the extent to which the assessment should look upstream of the process; assessment of natural feedstocks or their production may reveal unsuspected problems at the cradle stage, as in the case of the production of biodiesel from oilseed rape (Bull, 1996). Apart from product cleanliness in use and the utilisation of by-products (oil cake, glycerol), very large-scale cultivation raises two potential upstream problems: widespread pollen allergenicity; and, because Brassicaceous plants rarely form mycorrhizal associations, possible soil impoverishment and loss of mycorrhizal inocula from the soil following prolonged cropping. LCA does not consider economic factors, but this is an issue that requires further consideration. Guinee *et al.* (1993), for example, have argued that because of its quantitative nature, LCA may enable a trade-off between environmental impact and other elements, including cost components. Moreover, some equate clean technology with reduced risk as well as resource efficiency and waste minimisation. To what extent, then, should risk assessment be incorporated into LCA? Guinee *et al.* point out that LCA focuses on the actual inputs and outputs of the system under investigation and that the small accidents that occur in the underlying processes can be dealt with in annual averages. It does not cover the *intrinsic* risks of processes. Risk assessment, in contrast, deals with low-frequency, high-impact events. Consequently, this report does not include risk issues in the treatment of life cycle methodologies.

CONCLUSION: A GROWING ROLE FOR BIOTECHNOLOGY

This study is probably the first to pull together an overall picture of how modern process biotechnology is penetrating industrial operations. The advent of "modern biotechnology" may be taken as concomitant with the introduction of enzymes and recombinant DNA techniques into commercial processes. The pattern that emerges from the scattered data available on industrial biotechnology seems to be typical of the adoption of any new technology by society, a phenomenon that has been much studied over the years. Whether for internal combustion engines or transistors, the timing seems to be similar: an induction phase of about a decade, a period of rapid growth lasting about two decades, and then a period of maturation during which growth slows. Of interest is how to tell the difference between a technology that is in the early induction phase and one that will never truly lead to major and pervasive innovations. In biotechnology we see many relatively small applied examples, spread widely over many different industries. Some successful applications have been known for more than five years, others perhaps as many as ten, but the outlook is still unclear. There are certainly niches in which industrial biotechnology affords clear benefits, both economic and environmental, over existing technologies, and no major barriers to continued successes have emerged. At the same time, the power of the tool itself continues to grow, and in the end it is this capacity for self-improvement that must compel the judicious observer to forecast a very significant impact on many aspects of industry.

If we accept the proposition that biotechnology may penetrate manufacturing industries rather broadly, a separate issue is whether biotechnology-based manufacturing would be significantly cleaner than the alternatives. The *a priori* expectations of cleanliness come from the observation that living systems manage their chemistry rather more efficiently than man-made chemical plants, and that the wastes that are generated tend to be recyclable and biodegradable. On the other hand, significant waste and pollution were certainly characteristics of human activity in the 19th century, when much of our manufacturing was entirely biobased. What has changed is our ability to manipulate biological materials and processes through biotechnology. Chapter 4 shows that, in a number of cases where we can compare a biotechnology-based real world process with its alternative, biotechnology can deliver cleaner processes, but it is too soon to claim a consistent pattern of superior cleanliness in every case.

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CURRENT INDUSTRIAL APPLICATIONS OF BIOTECHNOLOGY*

- **Biotechnological operations are currently used in a wide range of major industrial processes.**
- **Applications tend to be industrial-sector specific; the report addresses chemicals and pharmaceuticals, pulp and paper, textiles and leather, food and feeds, metals and minerals, and energy.**
- **Economic competitiveness has been established for a variety of biotechnological applications to achieve cleanliness.**
- **Biotechnology-based processes have been successfully integrated into large-scale operations.**
- **Industrial penetration of biotechnology is increasing as a consequence of advances in recombinant DNA technologies.**
- **Biotechnological operations have led to cleaner processes with lowered production of wastes and in some cases lower energy consumption.**

INTRODUCTION

Biotechnology embraces a wide range of techniques, no one of which will apply across all industrial sectors. Nonetheless, biotechnology is so versatile that many industries that have not used biological sciences in the past are seriously exploring the possibility of doing so. Some patterns of use are beginning to emerge which suggest that the future economic impact of this technology will be significant. Moreover, concern about global warming and CO_2 emissions may play a role in this respect. However, a number of problems exist with regard to industrial applications. For example, the entrenched infrastructure in industries that have traditionally relied on physical and chemical technology presents a significant challenge to the widespread adoption of new biotechnology. Renewable feedstocks, once superseded by fossil fuel-based raw materials, are now making a comeback, in part because they are sometimes more accessible through biotechnological routes. New products from industrial biotechnology feature more functionality; the more sophisticated chemistries enabled by biological catalysts lend themselves to ‘‘smarter’’ products for the consumer at little increased cost.

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[*] This chapter was drafted under the responsibility of Dr. B. Marrs, President, Photosynthetic Harvest, Inc. (USA), with the collaboration of Dr. H. Doddema and M.B. de Hoop, TNO (Netherlands) for economic and statistical information. Contributors include: *industrial chemicals,* Dr. R. Dorsch, DuPont (USA); *drugs and other fine chemicals,* Dr. S. Takahashi, Kaneka (Japan) and Dr. D. Anton, DuPont (USA); *pulp and paper,* Dr. M. Akhtar, Biopulping International (USA); *textiles,* Dr. K. Clarkson, Genencor International (USA); *leather,* Dr. M. Griffiths, Mike Griffiths Associates (UK); *food processing,* Dr. K. Kraus, Fermentation Marketing (USA); *metals and minerals,* Dr. C. Brierley, Brierley Consultancy LLC (USA) and Prof. P.R. Norris, Univ. of Warwick (UK) for biomining/bioleaching; *energy,* Dr. M. Grossman and Dr. E. Stiefel, Exxon Res. and Eng. Co. (USA), and Dr. D. Monticello, Energy BioSystems Corporation (USA); *feed,* Dr. A. Morgan, Finnfeeds International Ltd. (UK), Prof. Dr. W. Leuchtenberger, Degussa AG (Germany), Dr. M. Eggersdorfer, BASF (Germany), Dr. H.P. Meyer, LONZA (Switzerland). The economic and statistical data were reviewed by a panel of biotechnology experts in the Netherlands, from industry (Dr. A. Bruggink, Chemferm; Dr. C. Buisman, Paques Bio Systems; Drs. Ing. A. Hooijmeijer, TNO Paper Production Technology; Drs. A. Luiken, TNO Industrie; Dr. M. van Oort, NOVO; Dr. M. van Vliet, British Leather Confederation; Dr. M. Warmerdam, Gist-brocades), government (Ir. M. Butter, Ministry of Housing, Spatial Planning and the Environment; Ir. J.J.M. Mulderink, DCO) and academia (Dr. J. Cramer, Eindhoven; Dr. W. Harder, TNO; Dr. L. Reÿnders, Amsterdam; Dr. W.H. Rulkens, Wageningen).

Box 2.1. **Biotechnology and CO_2 emissions**

Fossil carbon represents the single most important raw material for energy generation and for chemicals manufacture, but its oxidation product, CO_2, is an important greenhouse gas. Any means of reducing fossil carbon consumption, either by improving energy efficiency or by substituting alternative resources will directly result in lowered CO_2 production and thus reduce global warming.

Industrial processes

Use of biotechnology has already resulted in energy reduction in industrial processes. In only a few instances can the reductions be quantified, and these are presented in this report. Others are only available as anecdotal evidence. As yet, there are insufficient data to allow scaling up these figures to cover whole industrial sectors.

Ammonium acrylate, a key intermediate in the manufacture of acrylic polymers, is made by hydrolysing acrylonitrile to acrylic acid and reacting this with ammonia. The reaction is energy-intensive and gives rise to by-products which are difficult to remove. A process, based on a bacterial enzyme which directly synthesises ammonium acrylate of the same quality under less energy-demanding conditions, has been operating for several years at full scale.

In paper making, treating cellulose fibres in the pulp using cellulase and hemicellulase enzymes allows water to drain more quickly from the wet pulp, thereby reducing processing time and energy used for drying. Trials have shown that machine speeds can be increased by up to 7 per cent and energy input reduced by as much as 7.5 per cent. Replacing thermomechanical pulping by biopulping has resulted in up to 30 per cent reduction in electrical energy consumption.

Materials

Biomass, as it grows, consumes CO_2. Substances made from such renewable raw materials are therefore a zero net contributor to atmospheric greenhouse gases, unless fossil fuel is used in their manufacture. A wide range of chemicals and structural materials can be based on biological raw materials including biodegradable plastics, biopolymers and biopesticides, novel fibres and timbers. Plant-derived amides, esters and acetates are currently being used as plasticisers, blocking/slip agents and mould-release agents for synthetic polymers. Uses of biohydrocarbons linked to amines, alcohols, phosphates and sulphur ligands include fabric softeners, corrosion inhibitors, ink carriers, solvents, hair conditioners, and perfumes.

Clean fuels

While biomass can be consumed (incinerated) directly to produce energy, it can also be converted into a wide range of chemicals and liquid fuels. Although, in energy terms, annual land production of biomass is some five times global energy consumption, biomass presently provides only 1 per cent of commercial energy. Biomass energy cannot compete at present-day prices with fossil fuels and has so far penetrated the market only where governments have effectively subsidised its use.

Bioethanol is a CO_2-neutral alternative liquid transportation fuel. As new technologies – including continuous fermentation, production from lignocellulosic (wood and agricultural crop) waste – and more efficient separation techniques are developed, the cost of bioethanol will compete with that of gasoline. Over a 20-year period, US ethanol production, based solely on lignocellulosic waste, could rise to 470 million tonnes a year, equal to present gasoline consumption in energy terms.

This chapter examines current applications of biotechnology in the following sectors: chemicals (especially fine chemicals and pharmaceuticals); pulp and paper; textiles and leather; food processing (including animal feed); metals and minerals; and energy. These sectors have been chosen because they include many, if not most, of the most polluting manufacturing activities. The chapter considers a technology as applied if it has reached or passed the pilot stage of development. It also evaluates the economic contribution of biotechnology to cleaner industrial processes in these sectors.

Box 2.2. **Biotechnology-related sales (BRS)**

In this report, the term "biotechnology-related sales" (BRS) is used as the indicator of market penetration. Its coverage is defined in Chapter 1. Sales figures for biotechnology products, which are often used in economic studies, do not take into account the economic spin-off effects of these products when used for the manufacture of other products. This is especially relevant for process-integrated biotechnology. Therefore, in estimating the total market value of biotechnology, the conversion ratio of between 6 and 9 suggested by the European Association for Bioindustries (Ballantine and Thomas, 1997) is used for each of the selected manufacturing sectors world-wide. This allows for estimating a spill-over or ripple effect down the production stream for each sector.

CHEMICALS

The "chemicals" category includes the manufacture of commodity chemicals, pharmaceuticals, enzymes, refined petroleum and coal products, speciality and fine chemicals, and plastics. Chemicals manufacturing is a major generator of materials, a major consumer of energy and non-renewable resources, and a major contributor to solid, liquid and gaseous waste production. In the United States, for example, chemicals have consistently represented about 18 per cent of all manufacturing (based on sales) for the last 20 years (OECD, 1996).

Since biotechnology offers new ways of making chemicals, which may be cleaner than current methods, various sectors of the chemicals manufacturing industry have begun to experiment with the new tools. In terms of environmental impact, the possibility of using biobased resources as feedstocks in the larger volume sectors of the chemical industry is of particular interest. Although it is not certain that biobased manufacturing will always be cleaner than current methods when all environmental burdens are taken into account (see also Chapter 1), it is safe to say that wastes from biobased manufacturing will be more compatible with conventional wastewater treatment systems.

The slow penetration rate of biotechnology into the industrial chemicals sector suggests that the current overall economic advantage of biotechnology-based processes over existing methods is not enormous. The environmental advantages alone have not been sufficient to drive rapid adoption of biotechnology over existing chemical processes in this market. Penetration continues slowly, however, and the trend is clearly towards adoption of biotechnological tools in conjunction with conventional chemical tools to develop economically competitive new processes.

Biotechnology is prominent in the production of fine chemicals and pharmaceuticals, which account for about 1 per cent of the volume of products. World-wide, biotechnology used for cleaner production contributes about 60 per cent of total BRS value for fine chemicals and between 5 and 11 per cent for pharmaceuticals. In the United States, its contribution to the pharmaceuticals sector seems even higher, between 9 and 21 per cent. Biotechnology is increasingly being used to produce commodity chemicals (ethanol, acrylamide, organic acids) and chiral compounds. Pilot processes have been developed for the production of other substances, such as 1.3-propanediol.

The environmental efficiency of the chemicals industry has been improved by the application of biocatalysis, the recycling of solvents, and the (biological) treatment of wastewater. Biocatalysis represents about 60 per cent of the contribution to cleaner production. In the 1980s, biocatalysis was introduced into the production of fine chemicals and has resulted in a large reduction in waste production. As Table 2.1 shows, despite a four-fold increase in production volume, the production of waste was reduced by 20 per cent through the use of biocatalysis.

Commodity chemicals

It has been approximately ten years since the Nitto Chemical Company of Tokyo switched from a traditional chemical process to a biotechnology-based process for producing polymer-grade acrylamide. While the resulting environmental benefits have been widely reported, there are still relatively

Table 2.1. **Growth and efficiency in the chemical industry between 1975 and 1995**

	Increase in production volume Million tonnes	Decrease in waste production Tonne/tonne	Decrease in waste volume Million tonnes
Commodity chemicals			
– Petrochemicals	100 → 250	0.1 → 0.01	10 → 2.5
– Bulk chemicals	10 → 25	1 → 0.1	10 → 2.5
Fine chemicals	0.5 → 2	10 → 2	5 → 4
Specialities	0.1 → 0.5	50 → 10	5 → 5
Total (indicative)	100 → 300		30 → 15
Production + waste	130 → 315		315
Production/waste ratio	100/30		100/5

Source: Bruggink, Chemferm, Netherlands (personal communication).

few examples of the production of industrial chemicals by biotechnology-based processes. Nevertheless, it has been adequately demonstrated that biotechnological processes can be scaled up to the level needed for commodity chemical production.

Box 2.3. **Why biobased renewables?**

The rationale for using biobased renewables as chemical feedstocks is illustrated by several important advantages.

Biobased feedstocks are a major renewable resource today. The USDA [US Department of Agriculture] estimates that about 100 million acres of land would be available for growing energy crops in the 21st century. The rate of annual biomass replenishment has led several projections to conclude that biomass could supply almost all of [the United States'] domestic organic chemical needs.

Biobased and renewable resources represent an under-utilised segment of [the] nation's economy and could be produced in sufficient quantities to supply a large fraction of domestic chemical and power needs without adversely affecting traditional market outlets while diversifying the industry and increasing rural economic development.

Biobased renewables can be integral in building increased self-reliance for the United States. Chemical production incorporating a significant percentage of renewable materials is secure because the feedstock supplies are domestic, leading to a lessened dependence on international "hot spots". Events between Iraq and the United States in 1996 and the immediate response of the oil futures market are graphic examples of the hazards associated with dependence on politically unstable regions for crude oil.

Increased use of biomass will extend the lifetime of available crude oil supplies. Under a sustained growth scenario, the Royal Dutch/Shell group sees a biomass market in the first half of the 21st century of $150 billion a year, and estimated that 30 per cent of the world-wide chemical and fuel needs can be supplied by renewable resources during the same time period.

The use of biomass has routinely been suggested as an effective method to slow the build-up of greenhouse gases.

Biomass is flexible. The diversity of its building blocks from biomass offers just as much opportunity for the production of chemicals as do non-renewables. Suppliers of renewable feedstocks are less averse to the risk of producing non-traditional chemicals.

The economics of producing biobased feedstocks is often comparable to other conventional feedstocks and in some cases is superior.

Source: Personal communication, Dr. Gene Peterson and Dr. Joe Bozell, National Renewable Energy Laboratory, US Department of Energy.

A recent White Paper from the National Renewable Energy Laboratory (NREL) of the US Department of Energy (DOE), ‘‘Biobased Renewables 2020, A Vision for the Future: Maximising the use of one of our nation’s greatest natural resources’’, is particularly instructive in this connection. Box 2.3 contains excerpts from that document. Note that only one of the seven rationales presented for using biobased resources relates to environmental issues.

Whether or not the production of commodity chemicals from biobased feedstocks is cost-effective, petroleum feedstocks offer opportunities for using the tools of biotechnology for clean products and processes (see Box 2.4). Hydrocarbons can be metabolised by many organisms, and the partial oxidation products of hydrocarbon metabolism, including alcohols, acids, and epoxides, are chemicals that can be biologically produced from petroleum-derived materials.

Box 2.4. **Chemicals from biological feedstocks**

It is no longer necessary to start with a barrel of oil to produce chemicals. Corn, beets, rice – even potatoes – make excellent feedstocks. The fact that micro-organisms transform sugars into alcohol has been known for a very long time. But only since the advent of genetic engineering is it feasible to think about harnessing the sophistication of biological systems to create molecules that are difficult to synthesise by traditional chemical methods.

For example, the polymer polytrimethylene terephthalate (3GT) has enhanced properties compared to traditional polyester (2GT). Yet commercialisation has been slow to come because of the high cost of making trimethylene glycol (3G), one of 3GT’s monomers.

The secret to producing 3G can be found in the cellular machinery of certain unrelated micro-organisms. Some naturally occurring yeasts convert sugar to glycerol, while a few bacteria can change glycerol to 3G. The problem is that no single natural organism has been able to do both.

Through recombinant DNA technology, an alliance of scientists from DuPont and Genencor International has created a single micro-organism with all the enzymes required to turn sugar into 3G. This breakthrough is opening the door to low-cost, environmentally sound, large-scale production of 3G. The eventual cost of 3G by this process is expected to approach that of ethylene glycol (2G).

The 3G fermentation process requires no heavy metals, petroleum or toxic chemicals. In fact, the primary material comes from agriculture – glucose from cornstarch. Rather than releasing carbon dioxide to the atmosphere, the process actually captures it because corn absorbs CO_2 as it grows. All liquid effluent is easily and harmlessly biodegradable. Moreover, 3GT can readily undergo methanolysis, a process that reduces polyesters to their original monomers. Post-consumer polyesters can thus be repolymerised and recycled indefinitely.

Source: Advertisement published by the DuPont Company in *Scientific American,* May 1997, p. 22.

Commodity chemicals currently derived largely from plant matter in the United States include ethanol (3.8 billion kg/yr), cellulose esters and ethers (0.5 billion kg/yr), sorbitol (0.19 billion kg/yr), citric acid (0.16 billion kg/yr). A mixture of chemical and biotechnological approaches is currently used in this sector and represents the cutting edge of the impact of biotechnology on commodity chemicals.

Efforts to produce commodity chemicals such as succinic acid and ethylene glycol, which are currently made almost exclusively from petrochemical feedstocks, by using new processes and renewable resources, are in the pilot stage in government-sponsored programmes in partnerships with private enterprise (see Box 2.5).

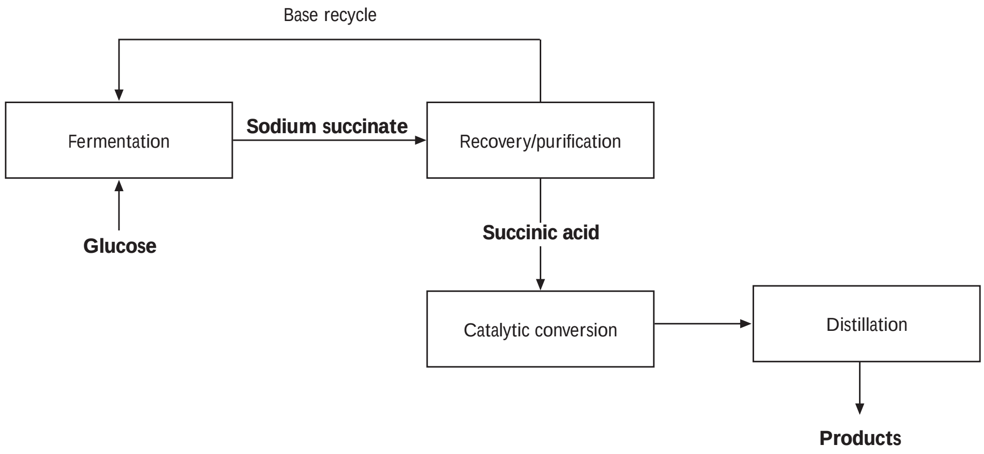
Box 2.5. **Chemical feedstocks from renewable resources**

Oak Ridge National Laboratory and three other US Department of Energy laboratories have signed a $7 million agreement with Applied CarboChemicals to manufacture chemical feedstocks from renewable farm crops at significantly lower cost than conventional petroleum-based methods while eliminating gypsum, an undesirable by-product that must be hauled to landfills.

The new process creates succinic acid by fermenting glucose sugar from corn, separating and purifying the acid and using it as an intermediate to produce 1.4-butanediol, tetrahydrofuran, N-methyl pyrrolidone and other chemical feedstocks used to make a wide assortment of products. Existing domestic markets for such chemicals total almost 0.45 billion kg – or more than $1.3 billion – per year.

Potential economic benefits of this and other projects of the Alternative Feedstock Program include expanded markets for corn and other renewable feedstocks, greater job security and perhaps job growth in agriculture and related industries. Energy savings may also be significant, as one combined biological and chemical plant producing chemical components could save energy equivalent to that needed to heat 80 000 single-family homes for a year and conserve valuable petroleum resources.

Process concept for chemical production



Source: Brian Davison, Oak Ridge National Laboratory.

Fine chemicals

The fine chemicals industry is one of the industrial segments where the impact of biotechnology (biocatalysis) is felt most strongly (Bruggink, 1996; Sheldon, 1997), owing to:

– the need to replace traditional stoichiometric processes to improve the product/waste ratio;

– the failure to translate chemocatalytic processes from petrochemicals to fine chemicals;

– the ready acceptance of enzymes by organic chemists;

– the low entry barrier, *i.e.* low investment, for new technologies in this small-scale industry;

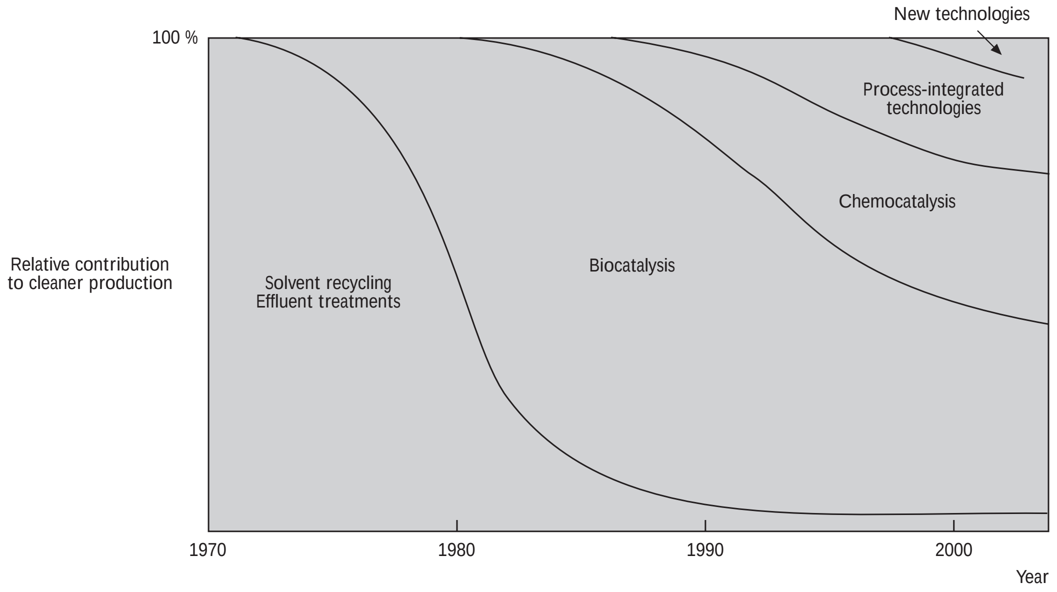
– the high specificity (including chiral specificity) and selectivity of biocatalysts.

While biocatalysis represents 60 per cent of cleaner production in the fine chemicals sector (Box 2.6), reuse and reduction of the solvents used has also contributed to more environmentally friendly production processes. As this is a small-scale industry, the absolute reduction for individual production processes is not large.

Box 2.6. **Clean production of fine chemicals**

For simplicity's sake, a production process may be subdivided into three steps: production of raw materials, conversion, and downstream processing. At present, biotechnology plays a role in conversion, in both fermentation and (immobilised) enzyme reactors. In the future, it can be expected to play a part in the production of raw materials, providing stock chemicals from biomaterials, and in agriculture as a primary production sector. Biosynthesis and fermentation processes, dedicated enzyme reactors, and selective biotechnological molecular recognition will also, in future, be more widely applied in downstream processing. In the conversion step, however, as the figure indicates, biocatalysis will have to compete with chemocatalysis, process-integrated technologies (PITs), and new technology.

Forecast of the relative influence of different technologies for cleaner production in the fine chemicals industry



Source: Bruggink, 1997 (personal communication).

Table 2.2 lists some products now being manufactured using biotechnology. As the table shows, there is significant biotechnological production of fine chemicals and pharmaceuticals. Vitamins are still mainly produced using organic chemistry, which remains the preferred method.

Enzymes

Enzymes are a special sub-set of the fine chemicals industry and have a large market volume (Table 2.3). They are applied in all manufacturing sectors; most often, they contribute to clean

Table 2.2. **Products and production volumes using biotechnology in the fine chemicals sector**

Tonnes per year

6-aminopenicillanic acid	7 000
7-aminocephalosporinic acid	1 000
Aspartame	600
L-lysine	280 000
L-threonine	10 000
L-methionine	200
Vitamin B12	12
Vitamin C	70 000
Provitamin D2	5
Vitamin F	1 000
Nicotinamide	3 000
D-p-hydroxyphenylglycine	3 000
Feed enzymes	20 000
Food-processing enzymes	100 000

Source: BUNR, 1996; Jihei Yoda, Japan Bioindustry Association, personal communication, August 1997.

Table 2.3. **Market size of enzyme sales to different sectors**

Million dollars

Detergents	300
Food and feeds	246
Paper	8
Textiles and leather	70
Total	624

Source: BUNR, 1996.

production or reduction of environmental pressure. Protein-removing enzymes in laundry detergents, which constitute the lion's share of enzyme sales, are an example of the latter. The environmentally beneficial effects of detergent enzymes are reduction of phosphate release into the environment and reduction in energy use during washing.

In 1996, market sales of enzymes for detergent applications world-wide amounted to $300-550 million, while the estimated total market sales of enzymes range from $624 million to 1.6 billion (BUNR, 1996; Novo Nordisk, 1997). However, all sources indicate that the enzymes in detergents are the largest contributor to enzyme sales. The US and European markets represent approximately 80 per cent of total world-wide demand for detergent enzymes. Based on enzyme sales for detergents, conservative estimates of total BRS for fine chemicals manufacturing can be derived (Table 2.4). Estimates of biotechnology's total contribution to cleaner production in Japan's chemical sector range between $1 billion and 2 billion (Ballantine and Thomas, 1997).

Health care products (pharmaceuticals, vaccines, diagnostics)

Today, many pharmaceuticals are semi-synthetic molecules in that part of their structure is synthesised by a living organism and that natural product is then modified by chemical processing. The recent design of thermostabilised enzymes and the development of a new bioreactor process by Kaneka Corporation have enabled the production of 2 000 metric tonnes/yr of a side chain for the production of amoxicillin. This all-enzymatic process has displaced an older one in which part of the synthesis was carried out chemically. The chemical part of the process had several problems, including colouring of the product, formation of by-products, and low energy efficiency. This is but one example of the application of biotechnology to improve process chemistry in the drug industry.

Table 2.4. **Estimated annual market share of biotechnology (BRS) in the chemicals industry**

Billion dollars

Sector	Europe[1]	United States	Japan	World
Total market value of chemical products	763[2]	511	452	1 726
Biotechnology value (BRS)	1-2[3]	1-2[3]	2	4-6
Biotechnology for cleaner production	1-2[3]	1-2[3]	1-2	3-6
Biotechnology for cleaner production (%)	1%[4]	1%	1%	1%

1. Estimates for Europe are based on market value in France, Germany, Italy and United Kingdom.
2. Excluding drugs and medicines.
3. Estimates based on sales of detergent enzymes.
4. Value of biotechnology's contribution to clean processes plus its contribution to the fine chemicals segment.

Source: Smith, 1996; Bickerstaff, 1995; Ballantine and Thomas, 1997; Abbott, 1996; Bijman, 1995; OECD, 1996.

According to European and US market studies, about 70 per cent of biotechnology companies operate in the pharmaceutical sector (US Congress, OTA, 1991; Ballantine and Thomas, 1997; Abbott, 1996; Smith, 1996; Degenaars and Janszen, 1996; Novo Nordisk, 1997). Greater use is made of biotechnology in the pharmaceutical industry for discovery of products than for manufacturing. However, many biotechnology products, such as diagnostic antibodies and gene probes, can only be produced using biotechnology. By definition, they cannot be classified as clean or cleaner, as they neither have zero discharge nor replace or improve existing technology. The product volume is generally very small.

There are indications, however, that clean biotechnological processes play a significant role in the health sector, in particular with regard to safer production of new and more effective vaccines (*e.g.* hepatitis, pertussis). In quantitative terms, antibiotics are the largest market segment (*i.e.* world-wide sales of penicillin of over $1 billion in 1996). They are produced using a mixture of biotechnological and chemical steps (Achilladelis, 1993).

Modern advances in biotechnology contribute to cleaner production of semi-synthetic antibiotics by biocatalysis, optimised fermentation, and replacement of organic solvents by water. For instance, by replacing a chemical reaction in methylene chloride by an enzymatic step in water, total use of methylene chloride was reduced by about 25 000 tonnes. Cleaner process-integrated biotechnology thus appears as important for the health sector as for other sectors.

In 1993, the total market for drugs and medicines in Europe amounted to $80 billion. Biotechnology contributes significantly to this segment, with a total indirect market impact of between $7 and $8 billion in 1996 (Ballantine and Thomas, 1997). Biotechnology's market share in cleaner production in the health sector therefore amounts to $4-6 billion (Table 2.5). In the United States, direct sales of biotechnology-related drugs and medicines rose from $6 billion in 1994 to $10 billion in 1995 (Bijman, 1995; Abbott, 1996). Total BRS for the pharmaceutical industry and the proportion of biotechnology used for cleaner production are estimated in Table 2.5.

Table 2.5. **Estimated market share of biotechnology (BRS) for pharmaceuticals (drugs and medicines)**

Billion dollars

Sector	Europe	United States	Japan	World
Total market value of drugs and medicines	80[1]	68	59	207
Biotechnology value (BRS)	7-8	11-18	3	21-29
Value of biotechnology in cleaner processes	4-6	6-14	1-2	11-22
Value of biotechnology in cleaner processes (%)	5-8%	9-21%	< 1%	5-11%

1. Estimates for Europe are based on market value in France, Germany, Italy and the United Kingdom.

Source: Smith, 1996; Ballantine and Thomas, 1997; Abbott, 1996; Bijman, 1995; OECD, 1996; Godfrey and West, 1996.

Crop protection chemicals

Biotechnology has enabled the production of known crop protection chemicals, such as glyphosate and chiral precursors or products. The DuPont Company has announced a new process for producing this popular broad-spectrum herbicide which uses enzymes cloned from spinach and yeast to create a catalyst capable of oxidising glycolic acid to glyoxylic acid, thereby greatly reducing the number of steps in the overall process as well as reducing loss of product to waste streams.

Because it is most like the drug discovery business, the search for new crop protection chemicals can benefit very directly from modern biotechnology. Traditionally, the discovery of new crop protection chemicals has relied on spraying samples of new compounds on test plants; this requires examination of tens of thousands of compounds to find one commercially viable new product and therefore high throughput screening methods. Micro-scale assays based on biotechnology, which save time and money, are currently being tested at virtually every major agricultural chemical company.

Purely biotechnological crop protection products, such as transgenic plants making bt-toxin, are coming onto the market. Bt-toxin is a protein produced by bacteria that are natural insect pathogens. This protein's toxicity is highly specific to the target insect species and therefore safe to use. First-generation biotechnology products using bt-toxin were simply preparations of bacteria and their spores, which contain the toxin, that could be applied to plants and ingested by insects. Current products were developed by cloning the toxin-coding genes from the bacteria into the crop plants, so that the plant produces the toxin. These new developments are at least in part a response to environmental concerns arising from the spreading of tonnes of bioactive chemicals on fields to control pests. Monsanto's first year of experience with transgenic cotton crops resistant to boll weevils seems to confirm the promise of a reduction in chemicals consumption through genetic engineering. Examples of other biotechnological developments addressing the needs of process chemistry are given in Annex 2.1.

PULP AND PAPER

The pulp and paper industry is a large and growing part of the world's economy. Pulp and paper production has increased globally, as has the rate of paper consumption. In general, the industry is very capital-intensive with small profit margins. To keep up with the increasing demand for pulp and paper and to meet increasingly stringent environmental regulations, the industry has been constantly looking towards technological improvements. (Annex 2.2 discusses technical aspects of pulping in greater detail.)

The current market size is probably only 1-2 per cent of total enzyme sales (BUNR, 1996; Godfrey and West, 1996). But, driven largely by market and environmental demands for less chlorinated products and by-products, the pulp and paper industry is cited as the fastest-growing market for industrial enzymes. In the United States it is projected to grow by 15 per cent a year for the next ten years. Cautious estimates indicate an enzyme market size of $14 million in the United States and $11 million in Europe in 1994. Table 2.6 indicates the contributions of biotechnology to clean production of paper and pulp.

Table 2.6. **Estimated annual market share of biotechnology (BRS) in the paper industry**

Billion dollars

Sector	Europe	United States	Japan	World
Total market value of paper products	311	362	227	900
Market value of biotechnology used in clean production	31-62	n.a.	n.a.	31-62
Market value of biotechnology used in clean production (%)	10-20%	n.a.	n.a.	3-7%

n.a. = not available

Source: Hooijmeijer, personal communication.

A variety of processes is used to separate the cellulose fibres from the lignin in wood and form a slurry (pulp) that is further processed into paper and board. Existing chemical pulping operations are particularly polluting. Biopulping, which is a cleaner process, involves the treatment of lignocellulosic materials with lignin-degrading fungi to manufacture the pulp. In the 1970s, Eriksson and co-workers at the Swedish pulp and paper research institute (STFI), Stockholm, demonstrated that fungal pre-treatment of lignocellulosic materials could result in energy savings and improved strength.

The economic feasibility of biopulping has been demonstrated at pilot scale; the process increases mill throughput by 30 per cent or reduces the electrical energy requirement by at least 30 per cent at unchanged throughput. An economic evaluation has been performed for a 600 tonnes/day thermomechanical pulp mill. Capital costs to incorporate this biopulping technology into a paper mill are estimated to be between $5 million and $7 million. Savings of $10 per tonne of pulp may be realised with 30 per cent savings in electrical energy. This is equivalent to an annual savings of $2 million, which, compared to the estimated capital costs, results in a simple payback period of two to three years.

Pitch is the mixture of hydrophobic resinous materials found in many wood species which causes a number of problems in pulp and paper manufacture. Traditional methods of controlling pitch problems include natural seasoning of wood before pulping and/or adsorption and dispersion of the pitch particles with chemicals in the pulping and papermaking processes, accompanied by adding fine talc, dispersants and other kinds of chemicals. During the past ten years or so, biotechnological methods have been developed and are now been used industrially. In the late 1980s, scientists in Japan discovered that the treatment of mechanical (groundwood) pulps with lipases, which catalyse the hydrolysis of triglycerides, reduces pitch problems significantly. In the early 1990s, Sandoz Chemicals Corporation in the United States (now Clariant Corporation) introduced a new product which is a fungal inoculum of the ascomycete *Ophiostoma piliferum*. Pitch, including toxic resin acids, is also metabolised quite effectively by lignin-degrading fungi in biopulping, which thus offers an additional benefit.

The structure and chemical composition of pulp fibre surfaces are of paramount importance for paper strength and other properties. Enzymes have been used to improve physical properties of fibres and might have a commercial role in future. For example, cellulases and xylanases can enhance pulp fibrillation and thereby improve paper strength. They can reduce fibre coarseness and increase paper density and smoothness.

The speed of paper machine operation depends in part on the drainage rate of water out of the pulp mat. Drainage rates tend to be lower for recycled fibres, so that the paper machine production rate decreases as the recycled fibre content increases. Cellulases and hemicellulases can improve the drainage rates of recycled fibres, and pilot- and mill-scale testing have led to the commercial use of these enzymes as drainage aids. Starch-modifying enzymes are sometimes used to improve paper quality. Enzymatic modification of starches is a cleaner process than chemical (oxidative) modification, as less energy is used and less waste is produced.

Traditional deinking processes use caustic soda, silicates and peroxide for oil-based printing materials such as newspapers and magazines. However, with the growing use of coating and new types of inks containing synthetic polymers in laser and xerographic printing, conventional deinking methods are inadequate for producing high-quality pulps. Recycling mills are therefore increasingly dependent upon mechanical devices to break down the larger non-ink particles to allow for removal by flotation or washing. Enzymatic techniques that allow for deinking of all kinds of recycled papers have recently been developed and commercialised.

The kraft process accounts for most of the world’s pulp production. Kraft pulps, however, have a characteristic brown colour, which must be removed by bleaching before the manufacture of paper for printing and writing or other products in which appearance is important. Traditionally, chlorination has been used, but because of consumer resistance and environmental regulations on chlorine bleaching, pulpmakers are turning to other bleaching chemicals (chlorine dioxide, oxygen, ozone, and peroxide), to extended pulping times, and to other process modifications. However, disadvantages associated with some of these methods are higher cost and/or greater danger of loss of pulp yield and strength as compared with chlorination.

A new method for whitening wood pulp has been developed at Haifa Technion in Israel and successfully tested in a large-scale paper mill trial. The essence of the process is a new enzyme which is better suited to the temperatures and pH found in pulp processing. The cost of the process is said to be the same as the conventional chlorine-intensive method. Studies conducted in Finland show that hemicellulases (mainly xylanases) enhance pulp bleaching. These enzymes are now being used commercially in Scandinavia, Canada, the United States, and Chile. The treatment of kraft pulps with xylanases leads to significantly reduced chemicals consumption, with almost no loss in pulp yield or quality. Biobleaching of acid bisulphite pulp with xylanases has also shown promise, with chemical savings of up to 51 per cent. Research is now being directed towards the discovery or engineering of enzymes that are more robust with respect to pH and temperature.

The most widely practised of the earlier biotechnologies are waste treatment processes. These are based in large part on the degradative activities of mixtures of aerobic and anaerobic micro-organisms, primarily bacteria. Advances in wastewater treatment applications have been in the engineering rather than the biological aspects. As environmental controls become stricter (*e.g.* the US Environmental Protection Agency's ''Cluster Rules''), it is likely that innovations will be made in biological as well as engineering aspects of wastewater treatment. The only long-term solution is likely to be the development of technologies that will allow mills to operate with zero effluent.

At present, cleaner production is largely achieved by process-integrated water treatment using biologically treated process water from the same production plant. Some 10-20 per cent of European paper producers reuse treated water in this way, so that there is zero discharge of wastewater (Hooijmeijer, personal communication). In the United States and Japan, a much smaller number of paper manufacturers use treated wastewater.

As Europe produces about 25 per cent of the world's paper, global market penetration of integrated water recycle is now about 5 per cent. This application of biotechnology lowers overall costs by sharply reducing the cost of fresh water intake and levies on wastewater discharge. In a small country like the Netherlands, if water cycles in paper manufacturing could be completely closed, this could result in annual water use savings of the order of 30 million cubic meters and an energy reduction of 3 million GJ (gigajoules). Energy savings would of course vary, depending on energy costs and environmental levies for each region. However, it is estimated that the potential for world-wide application would be about 200 times greater, *i.e.* 600 million GJ or 6 billion cubic meters of water.

TEXTILES AND LEATHER

Biotechnology, using enzymes, is becoming increasingly important in the manufacture of textiles and leather. Compared to conventional technologies, these are considerably cleaner processes. Table 2.7 indicates the market value of enzymes for textiles and leather and market value for clean production.

Textiles

Driven by globalisation and consolidation, the textile industry is undergoing significant changes. World-class R&D and manufacturing, coupled with the ability rapidly to identify, develop, and

Table 2.7. **Estimated annual market share of biotechnology (BRS) in the textile and leather industry**

Billion dollars

Sector	Europe	United States	Japan	World
Total market value 1994	273	239	160	672
Enzyme market value for textiles (BRS)	0.3	0.2	0.1	0.6
Enzyme market value for leather (BRS)	0.2	0.2	0.1	0.5
Market value of biotechnology used for clean production (BRS)	0.5	0.4	0.2	1.1
Market value of biotechnology used for clean production (%)	< 1%	< 1%	< 1%	< 1%

Source: OECD, 1996; Novo Nordisk, 1997; Godfrey and West, 1996.

commercialise new technology, are central to success. This has driven the textile industry to seek new sources of innovation, including biotechnology. Biotechnology has made significant contributions and more can be expected, since most textile fibres are naturally occurring or derived from natural substances. Natural fibres include: cellulosics, such as cotton, linen, ramie, and hemp, and proteinaceous fibres, such as wool and silk. Man-made fibres derived from natural substances include: lyocell, rayon, and cellulose acetate, all of which are made from wood pulp.

At present, the global market value of textiles is around $672 billion (OECD, 1996). In 1996, the global enzyme market for textiles amounted to $178 million (Novo Nordisk, 1997). The direct US market value of enzymes for textiles was $13 million in 1994 and $31 million in 1996 (Novo Nordisk, 1997; Godfrey and West, 1996). The total US market value of enzymes for the textile industry, taking into account indirect economic spin-offs, is estimated at around $200 million.

For Europe, the direct market value of enzymes for textiles was $28.3 million in 1994 and approximately $41 million in 1996 (Novo Nordisk, 1997; Godfrey and West, 1996). In terms of the total impact of enzymes on product sales of the textile industry, biotechnology accounts for approximately $300 million. Data for Europe and the United States have been used to determine the market size of biotechnology for clean production in Japan. As enzymes are used by a large section of the entire industry in the United States and Europe, it is likely that Japanese manufacturers also use them widely. It is estimated that Japan accounts for approximately $100 million of enzyme market value.

The application of biotechnology to natural fibres offers the opportunity to generate genetically engineered herbicide-resistant and pest-resistant plants, such as those produced by Monsanto to control bollworms and budworms, which can cause serious problems for the 20 million tonnes/year cotton market. Cotton is very vulnerable to insects and other pests; it is also prone to infestations by weeds and unfortunately has a poor tolerance to most herbicides.

Biotechnology also offers the opportunity to produce fibres with improved or novel features, such as Agricetus' genetically engineered cotton, which contains a bacterial gene that makes a polyester-like substance. The fibre is reported to have the texture of cotton, but to be much warmer. In addition, Monsanto, Calgene, Agricetus, DuPont, Bayer, and others are investigating possibilities of engineering cotton for increased strength, improved dye uptake and retention, enhanced absorbency, and wrinkle- and shrink-resistance. There is already a market for cottons naturally coloured through breeding techniques. However, the colour range is limited and could probably benefit from transgenic approaches. In the area of animal fibres, genetic studies on sheep and goats are being carried out in Australia (CSIRO) and elsewhere with the objective of producing fibres that are insect- and pest-resistant, softer, finer, more easily harvested, etc. In China, among other countries, methods to increase the viral resistance of silkworms and to overcome their dependence on mulberry leaves, as well as to improve the strength and fineness of the silk are being studied. Chitin and chitosan, which can be obtained from shellfish waste and some fungi, are receiving much attention in the area of wound healing. A calcium alginate fibre for use in wound healing has been developed by Courtaulds. Chitin is also being investigated as an absorbent for removal of colorants in waste streams.

Microbial production of fibres has also received significant attention. Zeneca has produced a naturally occurring polyhydroxybutyrate (PHB) by bacterial fermentation. The polyester is reported to have good thermal properties and can be spun into fibres. Monsanto is investigating genetically engineered plants for production of PHB. Other biopolymers with textile potential include polylactates, under development in Japan, and polycaprolactones, which are under investigation in the United States for medical applications. Weyerhaeuser and Ajinomoto have already produced a bacterially derived cellulose that is finer, more uniform, and more resilient than most cellulosics, and Sony has developed stereo speaker cones and diaphragms for headphones from bacterial cellulose. Several groups, including Protein Polymer Technologies Inc., Allied Steel, and Genex, have initiated programmes on microbial production of protein polymers. The initial focus has been on the hexapeptide repeat of *Bombyx mori* silk fibroin, the tripeptide repeat of mammalian collagen, and the decapeptide repeat of *Mytillus edulis* adhesive protein.

Another area of interest is microbial or plant routes to the production of biochemicals (including enzymes) and chemicals for use in the synthesis or treatment of natural, man-made, and synthetic fibres. DuPont, for example, has developed a microbially based fermentation process for the manufacture of 1.3-propanediol, a key ingredient in polytrimethylene terephthalate, a polyester that is superior to the widely used polyethylene terephthalate (PET), but which was previously too expensive to make in large amounts. In this case, the organism is engineered so that the carbon flow or pathway is optimised for the production of the 1.3-propanediol. There is also the possibility of using microbes and plants to produce textile auxiliaries and dyes. For example, Genencor International has developed a microbial process for producing indigo. In addition, Genencor International as well as Novo Nordisk and other enzyme manufacturers have invested in the production of enzymes which can be used in fibre preparation, pre-treatment to remove undesirable substances associated with the fibre, and finishing to modify the fibre properties and provide added benefits. Enzymes can also be used in biocatalysis processes and in waste treatment.

Enzymes have been used for decades by the detergent industry for cleaning and garment care. Although they have also been used in textile processing since the early part of this century to remove starch-based sizing, it is only in the past eight to ten years that serious attention has been given to the investigation of enzymes for a wide range of textile applications. One area which has had great success is the use of cellulases for the stonewashing of denim. In this case, enzymes are used in place of or in addition to pumice stone to create denim garments with a "worn" or faded look. Various appearances can be created by combining different cellulases and processes (see Chapter 4).

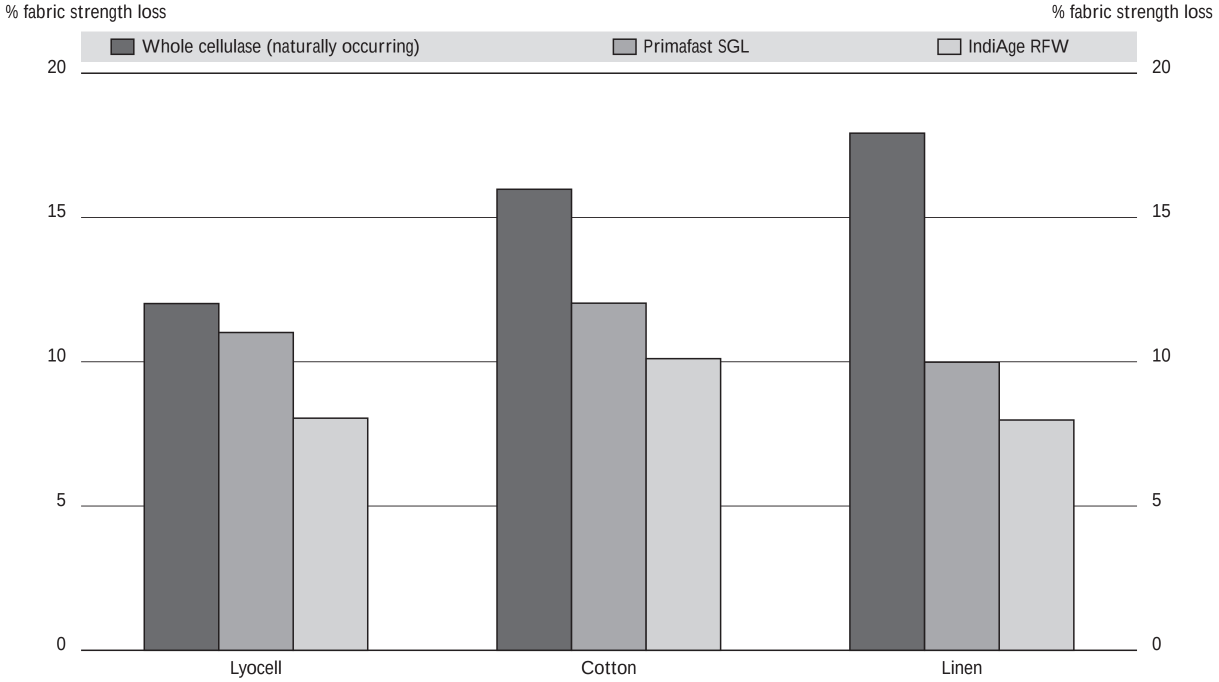
Similarly, in the late 1980s and early 1990s, other cellulose-based fabrics and garments began to be processed with cellulase, which can give superior "hand" and novel finishes on rayon, linen, and cotton knits and wovens. The benefits of cellulase treatment include: prevention of fuzz and pilling, increased smoothness and softness, increased lustre and superior colour brightness, improved handling and drape, and fashion wash-down effects. Cellulases are currently incorporated into a number of detergents for depilling or removal of surface fuzz as well as for maintaining colour clarity through many washings.

Cellulases are also gaining widespread use in the production of the relatively new fibre, lyocell, the generic name for solvent-spun cellulosic fibres. Lyocell is spun from wood pulp in a closed amine oxide solvent system. The solution is then filtered and extruded to form the filament. Compared to other man-made fibres (such as rayon), lyocell has greater strength and a more environmentally favourable manufacturing process. However, the fibre tends to fibrillate during processing. This fibrillation is unique to lyocell and can be controlled by cellulase treatment to achieve a soft, luxurious fabric hand and laundering fastness. In one case, lyocell fabric was treated with Primafast® SGL cellulase from Genencor International, which is an engineered cellulase composition designed specifically to achieve the desired performance.

Although cellulase offers many advantages for textile processing, there is the potential for loss of some fabric strength. The amount of strength lost is highly dependent on the type of cellulase used and the processing conditions. There is a wide variety of naturally occurring cellulases. Most are multi-component enzyme systems. The enzymes act synergistically to hydrolyse cellulose to glucose and other soluble sugars, which serve as a source of energy for the organism, or to nick and open the plant cell wall in order to provide the organism with access to the cell nutrients. In textile applications, however, hydrolysis of cellulose to glucose or destruction of the fibre is not the desired end result. Through selective screening of naturally occurring cellulase systems, genetic engineering of micro-organisms to produce tailored cellulase compositions, and protein engineering of individual enzymes to impart unique features, it is possible to achieve the desired performance benefits with little loss of fabric strength. Figure 2.1 sets the surface polishing benefit of a naturally occurring cellulase system and engineered cellulase compositions against fabric strength loss of several cellulosic substrates. The engineered (tailored) compositions [Primafast® SGL and Indiage® RFW (Genencor International)] clearly generate much less fabric damage.

Proteases also lend themselves to fibre modification. They have been used for several decades as cleaning agents in detergents and are now being investigated for use in wool and silk processing. Applications involving fibre modification of wool include anti-felting, depilling, improved dye uptake,

◆ Figure 2.1. ***Surface polishing vs. fabric strength loss***



Source: Kumar, *et al.*, 1996.

and softening. Felting is a unique property of wool caused by movement of the fibre and interlocking of the scale-like structure on a fibre's surface with the scales on neighbouring fibre surfaces, thereby preventing the fibre from returning to its original position. This occurs when the fabric is subjected to mechanical action in the presence of moisture. Not only do the scales cause felting, they can also cause irritation or a ‘‘prickling'' effect. Current processes used to control felting include chlorine treatment and the addition of polymer coatings to minimise the scales. Proteases are under investigation as a possible means of reducing or removing the scales. As in the case of cellulases, efforts are focused on achieving anti-felting benefits with minimal damage to the fibre. Proteases are also being investigated for surface polishing and softening of wool and silk.

Investigations are also under way on the use of enzymes in fibre preparation. Pre-treatment processes include: enzymes for removing sticky cotton; pectinases and hemicellulases for removing pectins and hemicelluloses associated with flax; pectinases, hemicellulases, proteases, and lipases for cleaning and scouring raw cotton; oxidoreductases and peroxidases for bleaching fibres; catalases for removing residual hydrogen peroxide associated with the fibre bleaching process; amylases for removing starch sizing agents (desizing); proteases for removing the protein-based gum (sericin) associated with natural silk and treatment of leather. This list is expected to grow and to be driven not only by value-added benefits but also by environmental factors.

Environmental benefits

Today, textile and apparel companies are spending more time and money on the environment. Regulatory pressure is expected to intensify as new technologies that offer alternatives to pollution and reduce waste become available. Some biotechnology alternatives – such as genetically engineered coloured cotton, organic cotton, and pest-resistant plants that eliminate or reduce the need for pesticides, artificial fertilisers, and harsh chemicals – already exist. However, to reach the market, transgenic crops must be approved by the appropriate regulatory agencies within the targeted countries. Currently, in the United States, up to three federal agencies may be involved: the Environmental Protection Agency, the Department of Agriculture, and the Food and Drug Administration.

"Stonewashing" of denim with enzymes instead of pumice stones is an example of environmental benefits (see Chapter 4). Enzymes are expected to have an even greater impact on effluent quality as more fibre preparation, pre-treatment and value-added finishing processes convert to biotreatment. Biotreatment may also be effective in eliminating biological oxygen demand (BOD) and removing and/or decolourising dyes in textile waste streams. Since enzymes are very effective catalysts even under mild conditions, they do not require the high energy input often associated with chemical processes. Therefore, in terms of the environment, biotechnology offers the opportunity to develop cleaner and more energy-efficient processes, produce higher quality products, and clean up effluents.

Leather

In 1996, total enzyme sales to the leather industry amounted to $80 million (BUNR, 1996). In the United States, leather process industrial enzymes constitute a $10.5 million market that is growing at about 2 per cent annually and is expected to reach $12.8 million by 2006. The use of enzymes in this industry has been reviewed by Taylor *et al.* (1987) and by Godfrey and West (1996).

Hides and skins contain proteins and fat in between the collagen fibres. Prior to tanning, these substances must be partly or totally removed. Proteins can be removed by proteases and fat by lipases, as well as by surfactants and solvents. Today, proteases are used mainly for soaking, bating, and enzyme-assisted dehairing. The use of lipases to dissolve and remove fat is still under development.

When preparing hides and skins, proper soaking of the raw material is necessary in order to obtain good quality leather. Some raw materials are stored dry and satisfactory rehydration may be a difficult and time-consuming process. With the use of proteases and carbohydratases to degrade interfibrillary protein and carbohydrates, water absorption is significantly improved and the soaking operation shortened.

The conventional way to remove hair has been to use chemicals such as slaked lime and sodium sulphide. These dissolve the hair completely and open up the fibre structure. However, the use of enzymes makes it possible to reduce the chemical requirements and, in addition, to obtain a cleaner product, a higher area yield, and fewer chemicals in the waste water. In particular, hair is not dissolved but can be filtered out, thereby reducing the chemical and biological oxygen demand of the waste.

Lipases are beginning to be used instead of solvents or surfactants for degreasing. The advantage of enzymes is that they interfere less with the skin structure. In addition, the enzyme process is more environmentally acceptable than solvent- or surfactant-based processes.

The degreasing of sheepskins is a recent introduction. Sheepskins have a world-wide market share of about 30 per cent of leather manufacturing. The enzymatic degreasing process replaces a paraffin solvent-based process and is therefore more environmentally acceptable. The recovery and reuse of paraffin involved high investment and running costs. Aside from its environmental benefits, enzymatic treatment also results in improved quality of the end product and reduced costs. The enzymatic process gives a product with improved tear strength and a more uniform colour (TME, 1994). By replacing solvent-based degreasing with enzyme treatment, costs can be reduced by at least 25 per cent, depending on the operational practice of a particular plant. The biotechnological process has a world-wide market penetration of 30-50 per cent. Large-scale applications are reported in Australia, England and France. However, the technology is not reported in southern Europe, an important production area for sheepskins.

In order to make leather pliable, it is necessary to subject the raw material to an enzyme treatment before tanning. During this process, known as bating, certain protein components are dissolved and can be washed away. The degree to which bating is applied depends on the desired softness of the finished product. Traditionally, dung was used as a bating agent; Pliny described the use of pigeon dung for this purpose more than 2000 years ago. In 1908, the German chemist Otto Röhm patented the first standardised bate based on pancreatic enzymes. Today, both bacterial proteases and trypsin (the traditional pancreatic protease) are used for bating, although fungal and plant enzymes have also been tried.

By using carefully chosen blends of enzymes to control the dissolution of individual skin components, such as elastin, it is possible to achieve subtle changes in the properties of the final product.

FOOD AND FEED

For Europe, the total estimated value of BRS in the food and beverages segment ranges between $10 and $17 billion (Smith, 1996; Ballantine and Thomas, 1997). Therefore, on the assumption that 50-80 per cent contribute to cleaner production, biotechnology's market value in the food industry ranges between $5 and $14 billion (Table 2.8). This represents all biotechnology, including traditional biotechnology as well as bioreactor technology, enzymes, and other advanced technologies. The use of enzymes is probably the largest application.

Table 2.8. **Estimated market shares of biotechnology (BRS) for the food processing, beverages manufacturing, and feeds industry**

Billion dollars

Market value*	Europe	United States	Japan	World
Total	717**	483	401	1 601
Total BRS	10-17	10-17	2	22-36
Clean biotechnology	5-14	5-14	1-2	11-30
Clean biotechnology/BRS (%)	1-2%	2-4%	< 1%	1-2%

* The total market size for the selected manufacturing sectors is based on OECD data related to total production, minus exports and plus imports.

** The estimate for Europe is based on market value in France, Germany, Italy and the United Kingdom.

Source: Smith, 1996; Ballantine and Thomas, 1997; OECD, 1996.

As no specific data were found on total BRS for the US food sector, these were estimated using total market size for the sector, and biotechnology's contribution was derived from enzyme sales in this sector in Europe and the United States. Data on actual market size for food enzymes in Europe and the United States differ. However, several sources suggest that the food enzyme market is similar in size in the United States and Europe, with total sales of $220 million for each region (Bickerstaff, 1995; Novo Nordisk, 1997; Godfrey and West, 1996). Therefore, total BRS in the US food, beverages and feed segment are estimated also to be between $10 and $17 billion. In the United States, biotechnology plays a greater role in food processing, beverages and feeds than it does in Europe, as US consumers more readily accept foods manufactured using modern biotechnology. For Japan, the total impact of biotechnology is estimated at $2 billion for a total food market of around $401 billion in 1993 (Ballantine and Thomas, 1997; OECD, 1996).

With a market penetration of between 2 and 4 per cent, the impact of biotechnology on clean industrial processes in the food industry is greatest in the United States. In Europe, the market penetration is between 1 and 2 per cent, while in Japan, it appears negligible to date. It is likely that biotechnology's actual impact is somewhat greater. Biotechnology is an important supportive tool for the food industry and can give considerable added value to the actual food product. However, changes such as the genetic modification of soybean are not included in the data presented here, and since soybean derivatives are used in more than 30 000 food products, the economic impact of this type of biotechnology product is considerable. The estimated contribution of biotechnology to clean industrial processes in the food, beverages and feed sector may therefore be conservative.

Food ingredients and additives

Proteins, carbohydrates, and fats are the basic food components in agricultural raw materials. It is theoretically possible to produce all three from alternate sources using microbial fermentation or plant tissue culture. The protein building blocks glutamic acid and lysine are already produced in large quantities by fermentation and used in animal feed (an agricultural application).

Single cell protein has received the most attention as a way to improve nutrition in developing countries, and, before oil prices rose in the 1970s, petroleum hydrocarbons were considered a desirable substrate. In the United States, Amoco and Phillips Petroleum developed processes based on yeast which were successful enough to produce yeast-based flavours but not economical enough to produce commodity protein ingredients. In the United Kingdom, Rank Hovis McDougall and ICI developed a process based on a *Fusarium* fungus and switched to a traditional (non-hydrocarbon) substrate. It was first approved for sale in 1985 and is currently marketed in Europe as Quorn mycoprotein by Zeneca's Marlow Foods subsidiary.

Among food biotechnology applications, production of basic food ingredients from non-traditional sources would have the greatest environmental implications because of the large volumes involved. Near-term developments are unlikely because of the relatively low cost of traditional ingredients (like soy protein) and the relatively high cost of alternate substrates (like petroleum hydrocarbons).

Food additives include gums, emulsifiers, vitamins, minerals, preservatives, leavening agents, acidulants, flavours, and colours. Consumer preferences for "natural" products give biotechnology-derived additives an advantage over chemically synthesised ones, if their cost is competitive. Examples of established biotechnology-derived additives from non-recombinant sources include xanthan gum from *Xanthomonas campestris* and citric acid from *Aspergillus niger*. One of the most discussed potential applications is the production of natural flavours (like vanilla) by plant tissue culture, although this has not yet had a commercial impact.

Fermentation-derived preservatives are another promising category. Most traditional food preservatives are chemically synthesised fatty acids or other organic acids that lower food pH and inhibit broad categories of micro-organisms. One trend is the development of fermentation-derived preservatives like "Upgrade" (developed by Stauffer Chemical and now produced in the United States by ICI's Quest unit) with the same active ingredient (propionic acid) found in chemically derived calcium propionate. Other fermentation-derived preservatives, like Delvocid (pimaricin), produced from *Streptomyces natalensis* by the Dutch company Gist-brocades, or nisin, produced from *Streptococcus lactis* by the Australian company, Burns Philp, have unique characteristics or applications. Bacteriocins like nisin are of particular interest because they can be produced by "friendly" lactic acid bacteria and are effective against especially challenging pathogens like *Listeria monocytogenes.*

The environmental benefits of producing food additives by fermentation or enzymatic routes instead of organic synthesis are similar to those for other speciality chemicals, *e.g.* reducing processing steps and the use of organic solvents. In the case of fermentation-derived preservatives, there is an even more favourable effect when the fermentation broth is incorporated in the finished product. The most desirable situation involves the use of bacteriocin-producing cultures *in situ* for fermented foods (like sausage or sauerkraut), where they consume unstable carbohydrates, naturally preserve the finished product, and contribute nutritive value of their own.

Processing aids, including enzymes, are usually added in small amounts for their functional effect during production but are not a significant part of the finished product. The global market for industrial enzymes is about $1.5 billion, of which about 10 per cent is for starch processing and 20 per cent for other food applications (Novo Nordisk, 1996).

Starch processing involves the conversion of corn or another grain into dextrose and other syrups by a hydrolysis reaction. This was formerly done using acid at high temperature and pressure, but dextrose yields were limited to about 80 per cent, and the process was hazardous and expensive and produced large quantities of salt as a by-product. The initial change to enzymatic hydrolysis in the 1960s increased dextrose yields and eliminated the drawbacks of the acid process. In the 1970s, development of immobilised glucose isomerase enzymes enabled the production of high fructose corn syrup. In the 1980s, thermostable alpha-amylases contributed to increased yields, and in the 1990s, recombinant thermostable amylases contributed to reduced costs.

Chymosin has been one of the recombinant food enzyme applications with the largest impact. Chymosin, or rennet, is the milk clotting enzyme used to make cheese. It was traditionally extracted from calf stomachs, but the gene for the enzyme was cloned in microbes so that it could be produced by fermentation. Pfizer began producing chymosin using *E. coli* bacteria in 1990, Gist-brocades followed, using *Kluyveromyces lactis* yeast in 1992, and Genencor International followed, using *Aspergillus niger* fungus in 1993 (Maryanski, 1995).

Baking is another area where enzymes have traditionally been used, in the form of barley malt to standardise the amylase (starch degrading) activity of wheat flour. Since the 1970s, fungal enzymes have partly replaced malt for this purpose. Different amylases with a specific "intermediate" temperature optimum came into use to retard bread staling in the 1980s, an application that has increased in the 1990s with the introduction of recombinant products. Combinations of glucose oxidase and other enzymes are being used to replace potassium bromate as an oxidant in flour for bread making because of concern about bromate's possible carcinogenicity. Recombinant and non-recombinant hemicellulases are being used to improve the processing and softness of whole grain and high fibre breads. Most recently, recombinant lipases have been introduced to replace or supplement the fat and emulsifiers used to give bread its volume and softness (Table 2.9) although all these enzymes are available from non-recombinant sources.

Table 2.9. **Recombinant food enzymes**

Product	Company	Trade name	Application	Year
Amylase	CPC International		Starch	1986
Amylase	Enzyme Bio-Systems	Megadex	Starch	1988
Amylase	Novo Nordisk	Novamyl	Baking	1990
Chymosin	Pfizer	Chy Max	Dairy	1990
Amylase	Novo Nordisk	Termamyl	Starch	1991
Chymosin	Gist-brocades	Maxiren	Dairy	1992
Chymosin	Genencor Int.	Chymogen	Dairy	1993
Xylanase	Novo Nordisk	Pentopan Mono	Baking	1995
Lipase	Novo Nordisk	Novozym 677	Baking	1995
Décarboxylase	Novo Nordisk	Maturex	Brewing	
Amylase	Gist-brocades	Dex-lo	Alcohol	
Amylase	Gist-brocades	Maxamyl	Alcohol	
Protease	Gist-brocades	Bakezyme	Baking	
Glucanase	Gist-brocades	Filtrase	Brewing	
Xylanase	Gist-brocades	Fermizyme	Baking	
Xylanase	Genencor Int.	Multifect	Food	
Xylanase	Röhm Enzyme	Veron	Baking	

Source: Dr. Kevin Kraus, personal communication.

One application with very great potential environmental benefit is the use of biotechnology to convert waste streams from one process into raw materials for another, or to upgrade under-utilised raw materials into a more valuable form. Ideas abound, including alternative uses for the grape pomace left over from wine making, corn cobs as a substrate for citric acid production, and cranberry waste as a substrate for fungal bioinoculants (Hang and Woodams, 1997; Pina *et al.*, 1997; Zheng and Shetty, 1997).

The dairy sector is especially promising, as large quantities of whey are produced from cheese making in centralised locations. One successful approach has been the production of *Kluyveromyces* and other lactose-fermenting yeasts as flavouring ingredients. Other attempts to hydrolyse lactose enzymatically so that it could be used in normal bakers' yeast have failed, and recombinant bakers' yeasts able to ferment lactose directly have not yet been commercialised.

Analytical techniques

Biotechnology techniques for food analysis are the same as those for clinical applications, but with uses both in process control and pathogen detection. Phenotypic methods, including immunoassay techniques, classify micro-organisms on the basis of on their behaviour and composition. They are useful for counting and separating pathogens into broad categories and have provided the basis for most food safety standards. The newer molecular subtyping methods, including polymerase chain reaction techniques, rely on the cell's unique genetic makeup to provide a different and more precise way of identifying pathogens. They can also be used to study specific strains within mixed microbial populations, making them especially useful for process control.

Even in developed countries like the United States and Canada, tens of millions of cases of food-borne illness occur each year. Because perishable products are processed and distributed quickly, speed is a major concern in detecting pathogens, but traditional culturing methods can take four days or more. By the time results are available, additional material may have been contaminated or the product may have been consumed. New immunoassay and molecular subtyping methods have an advantage, in that they provide results in hours instead of days.

Monitoring mixed microbial populations in complex environments like wine, yoghurt, sausage, or sauerkraut presents a unique challenge for process control. In such situations, traditional culturing methods are almost impossible to apply; new molecular subtyping techniques provide the first opportunity to understand and control processes we have long relied on.

DuPont's Qualicon subsidiary is applying molecular subtyping techniques to pathogen detection. They have commercialised the "Riboprinter", an automated system that uses restriction enzyme fingerprinting of ribosomal RNA to characterise bacteria and match them with a database. They also have several versions of "BAX", a polymerase chain reaction (PCR)-based quick test for detecting specific organisms on the basis of selected DNA fragments (Bruce, 1996).

The French company SigmO is also applying molecular subtyping techniques to process control applications in a joint venture with ITV (*Institut technique de la vigne et du vin*) and the Canadian company, Lallemand. They specialise in intra-species identification of yeast and bacteria, in particular to confirm the presence or absence of commercially important, non-pathogenic strains. SigmO uses a variety of techniques, including restriction analysis of mitochondrial DNA, alternating field electrophoresis, and PCR (Fleurent *et al.*, 1997).

There is the possibility of applying Qualicon's automation to SigmO's types of applications. Qualicon has developed a database for lactic acid bacteria, and researchers at the University of Florida recently reported on the use of the Riboprinter to monitor cultures in sausage and sauerkraut fermentation (Freund *et al.*, 1997; McCardell *et al.*, 1996).

In most cases, food processing applications involve the contained use of recombinant-derived organisms to produce an ingredient, additive, or processing aid which does not itself contain the viable organism. Food safety requirements usually dictate the use of non-toxigenic, non-pathogenic organisms, thus providing a further safety margin. Because the possibility of intentional or unintentional release of the organism in air, liquid, or solid waste streams remains, the same issues apply as for any other type of environmental release:

- survivability of the recombinant organism in the environment;
- host range of the organism used to express the transferred gene;
- substrate utilisation;
- competitiveness with other organisms;
- protein or polysaccharide production.

The general assumption is that when genetic material is moved between disparate organisms to produce intergeneric micro-organisms, there is greater risk that new traits will be introduced and that the behaviour of the new organisms is less predictable. There is in fact no evidence for this assumption, but it results in prudent precautions.

Again using recombinant enzymes as an example, organisms released as a consequence of normal production with commonly used hosts does not seem to raise an environmental issue. Data on one site with continuous incidental release of recombinant organisms in waste streams over a period of almost ten years showed no recoverable organisms and therefore no sign of their survival or establishment in the environment (Krause and Nayberg, 1997).

Feed

Modern biotechnology plays a significant role in the production of micro-ingredients for the feed industry, but in terms of volume and sales, chemically synthesised products have the major share of the total market. With the exception of some of the newer products, the micro-ingredient market grows roughly in line with the total feed market. In 1995, the volume of manufactured animal feed was 600 million tonnes. The market for poultry, pig and ruminant feeds is likely to grow steadily (up to 5 per cent a year) and that for aquaculture feeds more strongly (10-20 per cent a year).

The use of modern biotechnology for the production of amino acids, enzymes, vitamins and carotenoids, and other micro-ingredients for animal feeds is expected to increase. In addition, it is expected that nutritionally improved transgenic grains will affect the market for these micro-ingredients, possibly within the next decade. Since the common protein sources used in animal feeds (*e.g.* soya, fishmeal, wheat and maize) are deficient in methionine, lysine, threonine and tryptophan, these essential amino acids are added as supplements to monogastric diets, *e.g.* for poultry and pigs. To meet the need for these essential amino acids, it is possible to provide excess protein. However, the economical and more environmentally sustainable option is to use a minimum level of protein combined with supplemental essential amino acids. Whereas DL-methionine is produced by chemical synthesis (300 000 tonnes in 1996), L-lysine, L-threonine and L-tryptophan are produced by industrial fermentation using mutants of *Corynebacterium glutamicum* and recombinant strains of *E. coli.* The main producers of amino acids are Ajinomoto, Archer Daniel Midland, Degussa, Eurolysine, Fermas, Kyowa Hakko, Samsung and Sewon. In 1996, the market for amino acids in animal feeds was around $2 billion.

The production of L-lysine, which stood at 280 000 tonnes a year in 1996 and is growing at 7 per cent a year, is based on mutants of *C. glutamicum* produced by classical mutation and selection. The batch-fed production process is followed by separation of the broth from the biomass, purification from the broth by ion exchange, and finally crystallisation or spray drying as L-lysine hydrochloride. L-threonine production from *E. coli* constructs was 10 000 tonnes in 1996. Here again, after fermentation, the biomass is removed and L-threonine is then purified from the broth. L-tryptophan is the fourth limiting essential amino acid in pig and poultry diets. The biotechnological process and market are still in development. Recombinant *C. glutamicum* and *E. coli* strains have been constructed and are used, but the downstream processing is challenging (L-tryptophan is sensitive to oxygen and heat) and requires sophisticated know-how.

Feed enzymes are designed to degrade components of feed raw materials that limit digestibility and/or lead to a higher level of manure, nitrogen and phosphorus excretion. The best-known examples of feed enzyme products are those based on endoxylanases and phytases (see Box 2.7). Endoxylanase products depolymerise arabinoxylans present in wheat and maize, thereby increasing digestibility of all nutrients and reducing output of manure, nitrogen and phosphorus. Phytases hydrolyse phytic acid and release inorganic phosphate, thereby both avoiding the need to add inorganic phosphates to the diet and reducing phosphorus excretion. Other enzymes used in the feed industry include proteases, alpha-galactosidases, endoglucanases and alpha-amylases. Production micro-organisms used to manufacture feed enzymes include *Trichoderma* sp. (endoxylanases and endoglucanases), *Aspergillus* sp. (endoxylanases, phytases, alpha-galactosidases, proteases), *Humicola* sp. (endoxylanases and endoglucanases) and *Bacillus* sp. (proteases, alpha-amylases). Some of these enzymes are produced using recombinant DNA technology, but classical mutation and selection still play an important role. In the future, some feed enzymes may be produced from transgenic plants.

Box 2.7. **Enzymes in animal feed**

At present, animal feed is the fastest growing market for enzymes, with enzyme sales valued at around $120 million world-wide. For example, phytase is added to poultry and pig feeds to liberate phosphate from phosphate-containing compounds (phytates) in the feed. In pig farming, phosphate release in manure is reduced by 30 per cent. For a country like the Netherlands, this would result in a reduction of phosphate released into the environment of 20 000 tonnes a year. The price increase in the feed cost to farmers is marginal (about 0.2 per cent), and is compensated for by a reduced levy on the discharge of phosphate.

Source: TME, 1994.

Enzymes that survive high temperature processing conditions are a special need of the feed industry owing to the elevated temperatures generated during pelleting. Extremophiles are potential sources of such enzymes. Enzymes from exotic sources such as these will most probably be produced in micro-organisms more amenable to production.

The market for feed enzymes is growing strongly (by more than 25 per cent a year). In 1996, its global value was around $100 million. In 1997, some markets are close to saturation (enzymes for wheat- and barley-based diets for poultry), while others are growing strongly (enzymes for corn diets and the environmental sector), and new market opportunities are emerging for ruminants and aquaculture. The principal suppliers of feed enzymes are Finnfeeds (with Genencor), BASF (with Gist-brocades), Novo Nordisk, and Hoffman-La Roche.

In animal feed, vitamins are used to produce nutritionally optimal diets, which require all 13 vitamins and choline chloride. Most vitamins are supplied in special formulations to guarantee the stability and bioavailability of the product. The feed industry uses premixed vitamins optimised to meet the specific animal's needs. The market for all vitamins in animal feed (including choline chloride) represented about $1.4 billion in 1996 and was growing by 1-3 per cent. The important vitamins for animal feed are E, C, A, choline chloride, B_2, nicotinic acid, Calpane and B_{12}. The others are essential but less important in volume terms.

Vitamins are available today in sufficient quantities to meet the demands of the feed industry. Three major production methods are used:

- chemical synthesis;
- fermentation;
- extraction from plants or plant products.

The most important of these methods is chemical synthesis. In fact, with the exception of vitamin B_{12}, all vitamins are produced chemically. Vitamin B_{12} (cyanocobalamin) is produced exclusively through fermentation, since its structure is far too complex for industrial synthesis. Some vitamins, such as B_2 (riboflavin) and C (ascorbic acid), are produced biotechnologically as well as chemically. The main producers of vitamins are Hoffman-LaRoche, BASF, Rhone Poulenc and Takeda. For single vitamins, producers such as LONZA, Degussa and some Chinese companies have significant capacity.

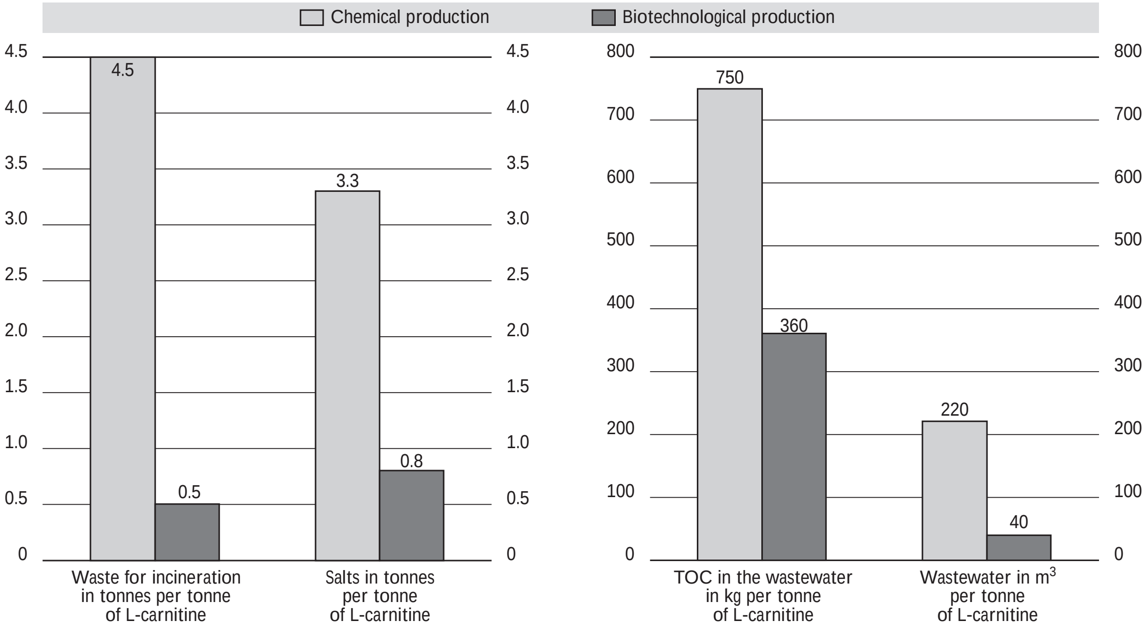
Vitamin E is produced semi-synthetically as a by-product of soybean oil production. In the process, a mixture of tocopherols is isolated through molecular distillation and chromatography. Its methylation yields the commercial product alpha-tocopherol. As a primary methyl donor, betaine is considered a quasi-vitamin and is produced by separation and crystallisation from beet molasses.

To produce vitamin B_2 (around 1 000 tonnes), different strains are used, such as mutants of *Ashbya gossypii, Candida flaveri, Bacillus subtilis* and *Corynebacteria.* Except for *Ashbya gossypii,* the strains are recombinant. The fermentation process is followed by separation of the broth from the biomass, purification and spray drying. Some 7-8 tonnes of vitamin B_{12} are produced by fermentation using *Pseudomonas* or *Propionibacterium* strains. After fermentation and filtration, the precursor is chemically transformed to cyanocobalamin.

The fermentation process for vitamin C starts from sorbitol (Chinese producers) or glucose and results in L-ketogulonic acid which, after isolation and purification, is transformed via a chemical step to vitamin C.

L-carnitine, an essential cofactor in the transport of long-chain fatty acids, is a significant new product for intensive animal production. A new biotechnological process developed by LONZA provides a rare comparison of waste generation by chemical and biotechnological processes producing the same product. Figure 2.2 shows a much cleaner biotechnological process, which produces about 50 per cent less total organic carbon (TOC) waste and less than 25 per cent of the wastewater as the chemical process.

◆ Figure 2.2. ***Waste treatment: chemical versus biotechnological production of L-carnitine***



Source: LONZA.

Carotenoids are used for pigmentation of salmonid fish (salmon, trout), broilers, and eggs. Those used in the feed industry are astaxanthin, canthaxanthin, citranaxanthin and C_3-carotenoids. They are produced by chemical synthesis or extracted from marigold (lutein) and paprika (capsorubin). The main producers of synthetic carotenoids are Hoffman-LaRoche and BASF. Several processes use algae (*e.g. Haematococcus pluvialis)* and yeasts (*e.g. Phaffia)*, with limited quantities available commercially. Possibilities exist for producing pigments biotechnologically using carotenoid pathway biosynthesis genes isolated from various bacteria, algae and higher plants (*e.g. Rhodobacter* and *Erwina* sp.). The market for carotenoids in animal feed is considered to be worth in excess of $500 million as of 1996.

METALS AND MINERALS

Biotechnology for mining and metals recovery can be divided into two major technologies: bioleaching/minerals biooxidation and metals bioremediation and recovery. These technologies are treated in more detail in Annex 2.3. The cleanliness of bioprocesses compared to conventional metal recovery methods has not been well established and would benefit from Life Cycle Assessment (see Chapter 4).

Bioleaching and minerals biooxidation are process technologies which are commercially employed world-wide by the mining industry for the extraction of base and precious metals. Bioleaching is the use of bacteria, principally *Thiobacillus ferrooxidans* and *Leptospirillum ferrooxidans* and certain thermophilic (high temperature) bacteria, to leach metals of value, such as copper, zinc and cobalt, from a sulphide mineral. During oxidation, bioleaching places the values of interest in the solution phase; the oxidation residues are handled for maximum recovery of the solution (within the volume and solution grade constraints of downstream processes), and the solid residue is discarded.

The operators of a copper recovery site in Chile claim as the principal advantages of bioleaching/ minerals biooxidation over more conventional processing technologies, including roasters, smelters, and pressure autoclaves:

- no noxious gases are produced (roasters produce As_2O_3 and SO_2, which must be contained);
- shorter construction time;
- environmental permits are acquired faster and environmental reporting is less onerous;
- no toxic effluents are produced;
- environmentally stable iron arsenate residue is produced;
- excellent metal recovery;
- simple and safe operation, as processing is at ambient temperature and pressure.
- smaller projects can be developed economically and have higher net present value (NPV).

The galvanising industry provides a good example of the use of biotechnology in clean production. Landskrona Galvanoverk in Sweden has designed a biotechnological process for metal finishing to replace the traditional alkaline degreasing process, which uses 5 per cent sodium hydroxide at pH 11-14. The alkaline process, which creates a large volume of wastewater containing heavy metals, has been replaced by an enzymatic degreasing process. The new process has also been implemented in two other galvanising companies. The environmental effects of the alkaline and the enzymatic process are given in Table 2.10, and the cost savings of the enzymatic process in Table 2.11.

Table 2.10. **Alkaline and enzymatic degreasing processes in the galvanising industry**

Material	Alkaline process	Biotechnological process
Waste	30 tonnes hydroxyde sludge	15 tonnes of hydroxide sludge
Feedstock	20% sulphuric acid	8% sulphuric and hydrochloric acid
Water	8 000 m^3	800 m^3

Source: Opinie, 1997.

The application of enzymes for degreasing galvanised metals has the environmental benefits of reduced operating temperature, reuse of tensides, prolonged life of degreasing and pickling baths, reduced water and acid consumption, reduced waste generation and better process performance. The simple payback time is estimated at five years. The process may have some disadvantages, such as consumption of tensides or production of metal-containing sludge, which will have to be further analysed during the first years of full-scale industrial application.

Table 2.11. **Annual savings on degreasing operating costs Enzymatic vs. alkaline process**

Catgory	1990 dollars
Water	10 800
Chemicals	
– Inhibitor	10 100
– Degreasing agent	7 800
– Sulphuric acid	6 700
Electricity	7 100
Maintenance	37 800
Total	80 300

Source: Opinie, 1997.

ENERGY

Biotechnology has had a major effect on the economics and environmental impact of the energy sector. It has improved the overall efficiency of processes, particularly in the area of pollution control. Processes currently under development, such as biodiesel, bioethanol and biodesulphurisation, seek to replace systems that are more energy-intensive and generate less benign by-products. The effect of genetic engineering on these technologies will be great, but it has yet to have a dramatic impact.

In terms of their cleanliness and sustainability, fuels represent a continuum of energy resources. The least clean energy resources are wood and the fossil fuels, coal and petroleum. Fossil fuels are also the least sustainable, and petroleum reserves in particular are declining. Coal reserves are higher, but coal produces more environmental contaminants when mined and combusted than petroleum. Biotechnology has the potential for producing cleaner coal and petroleum, primarily through the removal of sulphur, and therefore for reducing the environmental contaminants released during combustion. The production of low sulphur fuels will extend the reserves of fossil fuels that can be employed as energy sources and reduce the levels of air contaminants. Biotechnology also has the potential to produce equivalents to petroleum distillates, such as biodiesel, which could contribute to the sustainability of these fuels as energy resources. Ethanol, methane, and molecular hydrogen are even cleaner energy resources. The production of these cleaner fuels can potentially be sustained by biological production coupled with conversion of solar energy. Bioproduction of these cleaner energy sources could result in greatly lowered levels of greenhouse gases (see Box 2.1 above).

Opportunities for biotechnology to affect the energy sector involve both the fossil-based and biomass-based fuel industry. Since these fuels are biological in origin, they are particularly amenable to bioprocessing. Ethanol and methane are prime examples of fuels produced biologically from biomass. The application of biotechnology to the energy sector has been an area of very active research and development for the past several decades. Until very recently, these applications relied upon naturally occurring microbial strains, either as uncharacterised consortia of microbes or as pure cultures. Despite over 20 years of research, large-scale application of genetically engineered strains has only begun in the last five years. In general, these applications rely upon harnessing and amplifying particular metabolic activities of the bacteria, such as the capacity to transform sugars to ethanol, carbon dioxide or surfactants and to degrade trace amounts of toxic organic compounds into harmless compounds. Examples of these and other applications are outlined below.

Alternative energy sources

The oldest example of the use of "biofuels" is of course the burning of wood, peat, coal, and petroleum products. Supplies are not inexhaustible, and in recent years efforts have been made to develop cleaner, renewable sources of energy using modern chemical and biotechnological processes.

Currently, most biomass-derived ethanol for fuel is made from sugar cane, corn and other starch crops. In the United States, approximately 3.8 billion litres of ethanol are produced annually and production in Brazil may be four times as much. However, a tax credit is needed to achieve a competitive market price. To be economically competitive with fossil fuels, the technology for producing ethanol from biomass-derived sugars will require using high-yield low-cost crops and more efficient methods of converting lignocellulosic waste material into fermentable sugars. These two areas are the focus of current research.

US Department of Energy (DOE) researchers are examining dedicated energy crops, wood, and grass species which have been selected to produce high yields. They estimate a potential availability in the United States of approximately 2.5 billion metric tonnes of cellulosic biomass each year for fuel conversion, for a potential ethanol yield of 1.02 trillion litres. This compares favourably with the annual US consumption of transportation fuels (253 billion litres of gasoline and 82 billion litres of diesel in 1995).

Scientists involved in DOE-sponsored studies at the National Renewable Energy Laboratory (NREL) are targeting a procedure known as simultaneous saccharification and fermentation for converting cellulose to ethanol. The process combines the cellulose hydrolysis and fermentation steps in one vessel to produce high yields. Advances in genetic engineering are also making the fermentation of hemicellulose sugars more productive. The objective is to develop, by the year 2000, technologies for producing ethanol from biomass at a cost that will be competitive, without tax incentives, with the cost of gasoline. DOE reports that the studies so far have resulted in improvements that reduce the predicted cost of biomass-derived ethanol from $0.95/l to $0.34/l.

Biodiesel is an alternative renewable energy source derived from the de-esterification and methylation of soy or rapeseed vegetable oil. It is already produced commercially in small quantities in Europe and Japan with significant government subsidies. Because of its high cost, which often exceeds $0.80/l, it cannot currently compete with petroleum-based fuels. NREL is investigating low-cost sources of biodiesel, such as recycled grease from restaurants and inedible fats from the rendering industry. However, it is unlikely that biodiesel will replace a significant percentage of the demand for diesel. For example, the entire 1995 US soya crop, approximately 60 million acres of cultivated land, would have produced 11 billion litres of biodiesel, only 13 per cent of the total diesel demand. Information on biodiesel may be found on the National Biodiesel Board website (http://www.biodiesel.org).

The bioconversion of synthesis gas to liquid fuels such as ethanol is also being investigated. Synthesis gas is a mixture of CO, H_2 and CO_2 made by the partial oxidation of any carbonaceous material. Feeds for the production of synthesis gas include agricultural, municipal, and paper wastes and coal, natural gas, or biomass grown specifically for this purpose. The range of feeds for synthesis gas make it a particularly versatile source of fuels. With potentially lower processing costs and greater carbon yield, fuels derived from synthesis gas are an attractive alternative to fuels produced by fermenting biomass-derived sugars. Chemical routes involving processes of the Fisher-Tropsch type also exist for converting synthesis gas into chemicals and fuel range hydrocarbons. This indirect technology requires strict H_2/CO ratios, and efficient operation is sensitive to sulphur gases above 0.1 ppm and requires high temperatures and pressures (225-365 °C, 2.5 MPa). Bioconversion of synthesis gas, by comparison, does not require purification of the gases, high temperatures, or high pressures.

Research sponsored by DOE, the National Science Foundation, the Electric Power Research Institute, the Gas Research Institute, and others has led to improved understanding and productivity for the biological production of fuels and chemicals from synthesis gas. The biological process has been shown to be efficient, and residence times of a few minutes have been obtained for virtually complete conversion of H_2 and CO. Preliminary studies from DOE's Office of Industrial Technologies show that methanol can be produced for under $0.10/l.

The high cost of large-scale production of biogas (methane plus CO_2) as compared to prices for other fuel sources is the main factor limiting the introduction of biogas production as an alternative energy source for industry and for electricity. Biogas and alcohol production are comparatively more expensive than non-renewable energy sources. Although production prices for biogas are not as high as those for alcohol, biogas is of lower combustion quality than other sources of energy.

Spelman (1994) indicates that the cost of agricultural raw materials is too high to replace oil-based products. The underlying economic trend is, however, in agriculture's favour: oil will eventually rise in price whereas agricultural raw materials are renewable and are becoming progressively cheaper relative to oil. For instance, one tonne of oil would buy four times as much wheat in 1990 as in 1967.

Biodesulphurisation

The microbial desulphurisation of fossil fuels has been under active investigation for over 60 years for two reasons. One has been to understand the fate of these molecules in the environment, as they represent an important and recalcitrant component of crude oil spills. The other has been to develop processes for pre-combustion removal of sulphur from coal, crude oil and petroleum distillates.

Sulphur must be removed from fossil fuels because the combustion of sulphur molecules in coal and petroleum products leads to the production of sulphur oxides. These corrosive compounds are the source of acid rain and have a significant impact on the global environment. Biodesulphurisation is intended to replace an existing process (hydrodesulphurisation) which is expensive, energy-intensive, and relatively inadequate for the deep desulphurisation of fuel that will increasingly be required as low sulphur crude becomes scarcer and regulations become more stringent. The undesirability of sulphur in fossil fuels has already led throughout the world to increasingly stringent regulations on the content of sulphur in fuels (Table 2.12).

Table 2.12. **Recent and pending sulphur regulations**

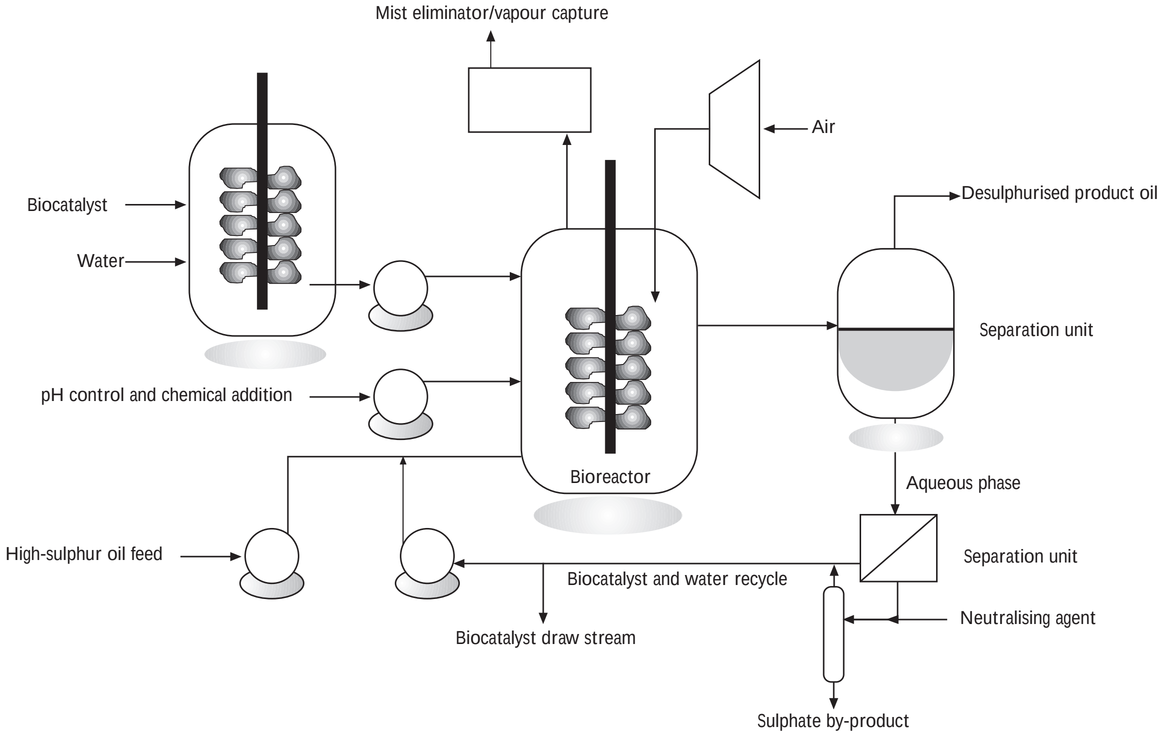
Sulphur levels (ppm)

Year	Country and fuel	Current	Target
1993	United States – on-highway diesel	2 500	500
1996	Singapore – diesel	5 000	2 500
	India – diesel	8 000	5 000
	European Union – diesel	3 000	500
1997	Japan – diesel	2 000	500
1998	Chinese Taipei – diesel	5 000	500
1999	European Union – heating oil	3 500	1 000
	European Union – bunker oil	33 000	10 000
2000	Korea – diesel	2 000	500
	Thailand – diesel	5 000	500
	European Union – diesel	500	350
	United States – CAAA gasoline	400	50-100
	European Union – gasoline	500	350
2005	European Union – diesel	350	< 100

Biodesulphurisation of crude oil and its fractions (gasoline, diesel, etc.) involves the application of microbial cells to the fuels and the use of their metabolism to transform the sulphur atoms into water-soluble products which can be extracted from the oil. The enzymes involved in this metabolic system have been isolated and characterised, and the associated genes have been cloned and over-expressed in new microbial host strains. The new organisms have been genetically engineered to create microbes which manifest desulphurisation activity 100 times higher than that found in the natural isolate.

Figure 2.3 presents the basic application of these biocatalysts. The bacteria are produced in conventional fermentation facilities and then introduced into a refinery's desulphurisation reactor, for example. The high sulphur oil and water are also introduced. In the reactor, the bacteria metabolise the sulphur-containing hydrocarbons and produce the water-soluble sulphur products. These are then extracted into the water phase. Following the reaction, the phases are separated and the desulphurised oil is removed for further processing. The biocatalyst and the water are recycled to the reactor for further use. A side stream of water and spent catalyst are continually removed from the reactor to be replaced by fresh catalyst and water. The sulphate-laden water can then be treated in the refinery and disposed of in conventional ways.

◆ Figure 2.3. ***Biocatalytic desulphurisation process***



Source: Energy BioSystems Corporation.

This technology is currently being scaled up to commercial level. At present, the largest unit is a five barrels/day pilot-scale unit operated by Energy BioSystems Corporation in the United States. They predict commercialisation of the technology in the next few years for diesel and in three to five years for crude oil. It has the potential to rival ethanol production as the largest process application of biotechnology in the energy sector and to have a significant impact on the economics of fuel processing. Like ethanol production, however, it must compete with existing solutions and faces daunting economic challenges before becoming a widespread technology.

Enhanced oil recovery

The application of biotechnology for recovering additional oil from in-ground crude oil formations has been the object of R&D and actual applications for at least 30 years. In certain cases, this can improve the environmental performance of the extraction process. Three major applications have been successfully implemented. The first is the use of "biosurfactants" produced by oil-degrading bacteria. These bacteria are produced through standard fermentation procedures under conditions that cause them to secrete surfactants which can then be injected into crude oil formations. There, the surfactants solubilise residual oil that was not released in the initial pumping operation, thereby resulting in "enhanced" oil recovery from the well. Similarly, some bacteria produce polymers, such as xanthan gum, which can control the viscosity of flood solutions during secondary oil recovery. Modified strains of *Xanthomonas campestris* that make gum varieties with altered properties have been explored but not commercialised.

Bacteria or bacterial products are also used to modify the formation itself. In this case, the bacteria are injected into the well and allowed to grow. As a result, they form carbon dioxide which repressurises the formation and forces more oil to the well. Bacteria or the polymers they produce are also used to plug a formation, thereby directing the oil flow in the desired direction.

Microbial dewaxing is another example of the use of bacteria to increase crude production. In this case, particular microbes, and perhaps some nutrients, are pumped into the well where they grow at the expense of certain components of the oil. These hydrocarbon-degrading bacteria can metabolise long-chain alkanes (waxes), thereby reducing the viscosity of the oil and leading to increased flow from the well.

While microbially enhanced oil recovery has been practised through out the world, it is not an exact science, owing to the many variables associated with different crude oil formations, the oil itself, and the poorly understood nature of the bacteria.

Box 2.8. **Clean industrial processes should be encouraged**

It might be assumed that reduction of raw materials, energy consumption and wastes is so clearly translatable into reduction in cost that any such process would immediately find an industrial application. Nevertheless, only a few such processes are in operation and the reasons are understandable: novel processes often require high capital expenditure and process development costs which outweigh any reduction in operating costs. For example, the scale of recovery of added-value materials from waste may be so small, and the downstream process costs so high, that the overall process is uneconomical even when the raw materials are "free". It should be borne in mind that a conventional processing plant is built to operate for many decades and the reduced costs of a novel process have to show a positive return in comparison with the low costs of a fully depreciated plant.

A second reason for hesitating to include a novel process is the difficulty of integrating it into a an existing, multi-stage process. In the pharmaceutical area, for example, not only is the finished product registered with the authorities before sale, but so is the complete manufacturing process. Any change to the latter therefore requires a new registration. Only when the new process can easily be integrated, as in the case of wet-strength resin manufacture (see Chapter 3), is it readily accepted.

A third reason for the slow penetration of biological processes is more sociological in nature. The traditional education of chemical engineers and chemical plant designers does not include biological processes. The nature of the materials, the vessels and the operating conditions are so different that engineers and plant operators require complete re-training and are therefore much less likely to have the confidence they have with more familiar process elements.

Where the economic advantages are overwhelming, as they are in cases of early adoption, industry will require no further persuasion. However, there may be a role for government in helping the new technology over the initial barriers to acceptance. In part, this role will be educational in nature – informing industrial management, re-training operatives, advertising the advantages to the general public. There may also be an economic role whereby, in the short or medium term, new technology is given selective advantage via the tax system or financial encouragement is given to demonstration projects for new products and processes. A third role is more overtly regulatory, as when industry is required to adopt cleaner technology for its wider environmental benefit, regardless of the increased initial cost.

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SCIENCE AND TECHNOLOGY TRENDS AND POTENTIAL*

- **The development of clean products and processes is influenced by public demand, market pull, and scientific and technological feasibility.**
- **Among the emerging science and technology discoveries that present major opportunities for developing clean biotechnological products and processes are improved and novel biocatalysts, bioconsortium-based systems, pathway engineering, and bioinformatics.**
- **The introduction of biotechnology into many industrial processes will be increasingly dependent on the development of recombinant biocatalysts.**
- **Bioprocessing engineering and integrated bioprocessing also remain as critical factors for the commercialisation of biotechnology.**
- **Various technical bottlenecks need to be overcome through R&D in order to increase biotechnology's penetration into industry.**
- **Demonstration projects are vital for bridging the gap between laboratory biotechnological research and industrial implementation.**

INTRODUCTION

As the previous chapter made clear, biotechnology already contributes to clean manufacturing in many industrial sectors. The present chapter first estimates short-term trends in this market, and points to the contribution of clean biotechnology to the different sectors for the next decade. The market forecast indicates the need to address the technical issues that create bottlenecks and obstacles to the further deployment of biotechnology for cleaner products and processes. This chapter therefore examines these issues as well as the opportunities that are arising as a result of technical developments.

Between 1995 and 2000, biotechnology-dependent sales in the area of human/animal health are expected to double to reach around $35 billion and in that of food to reach some $18 billion. In the area of equipment/diagnostics, the firms involved anticipate an increase from $8-9 billion at present to around $20 billion by the end of the decade. For chemicals, the increase is expected to be even more dramatic, rising from around $5 billion to some $15 billion over the same period (Smith, 1996).

Table 3.1 gives present estimates and forecasts to 2005 for the share of total BRS (biotechnology-related sales – for definitions see Chapters 1 and 2) for selected sectors, world-wide. Future estimates are mainly based on enzyme market studies. Some analysts predict a 19 per cent average annual growth in product sales between 1996 and 2006 for speciality areas of biotechnology, including industrial enzymes.

The enzymes market and its predicted growth for different sectors may be used as another indicator of biotechnology's growth potential (Table 3.2). These data indicate that the impact of biotechnology may double over the coming years.

In order to understand the possibilities for developing environmentally friendly products and processes, and to clarify which areas of research require effort, it is necessary to examine public demand, economic demand (or market pull) and scientific and technological feasibility. These three

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* This chapter was drafted under the responsibility of Dr. R. Kurane, National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology, Ministry of International Trade and Industry (Japan).

Table 3.1. **Market share of biotechnology (BRS) for selected sectors, world-wide**

Total BRS as percentage of total market value of products

Sector	1996	Forecast 2005
Chemical products[1]	< 1%	< 1%
Pharmaceuticals/fine chemicals	5-11%	10-22%
Pulp and paper	5%	35%
Food	1-2%	2-4%
Textiles	< 1%	< 1%
Leather	< 1%	< 1%
Energy	< 1%	< 1%

1. Excluding pharmaceuticals (drugs and medicines, human health care products).

Source: Compiled and adapted from various sources.

Table 3.2. **Estimated trends in industrial enzyme markets (United States and Europe), 1995-2000**

Million dollars

Area	1995	2000
Detergents	280	400
Food	240	370
Beverages	200	320
Other	160	320
Total	880	1 410

Source: Bickerstaff, 1995.

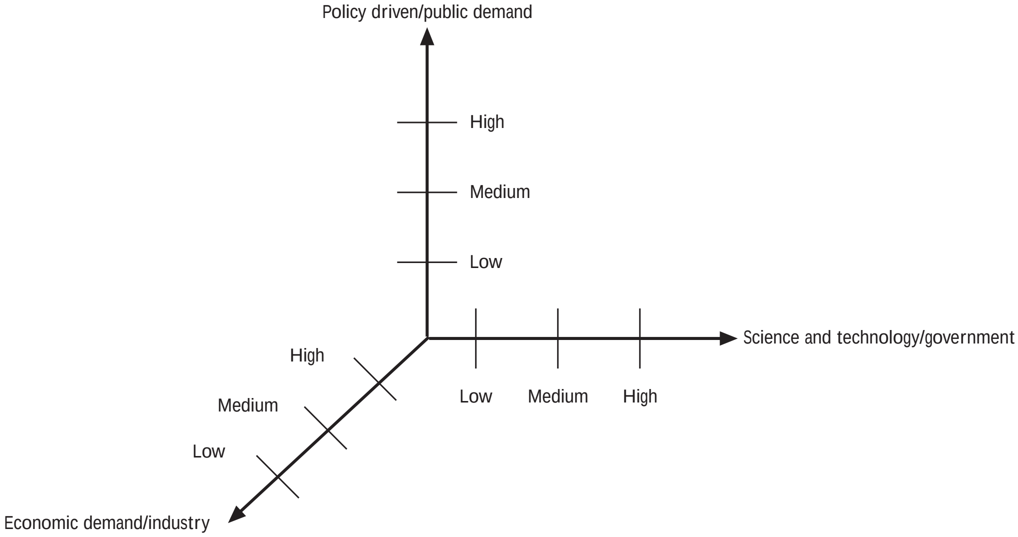
parameters can be regarded as representing the three major stakeholders: the general public, industry, and government, respectively. Depending on the particular stakeholder, each of the three parameters may be given a weighting as illustrated by the axes of Figure 3.1. The priorities (weightings) for these parameters will differ from country to country. Industry may emphasise cost aspects and might, for example, welcome the incorporation of a new unit stage into an existing process, thereby avoiding the cost of designing and commissioning an entirely new process.

Changing public and governmental attitudes to the environment as well as to the potential usefulness of R&D developments offer many opportunities for the introduction of “green” products and processes. Scientific and technological bottlenecks that are hindering the development of new biotechnological products and processes must also be considered when evaluating these opportunities.

It is impossible, in a report of this nature, to cover in detail the fundamental science underpinning novel biotechnological developments. It is difficult to identify those aspects of R&D which relate solely to cleaner products and processes, since much of what is described in this chapter, particularly in advanced areas such as genomics and informatics, underlies progress in all sectors of biotechnology, from medicine to agriculture. In illustrating these areas, good examples are presented, even where they do not relate exclusively to clean technology.

Although this report takes pains to underscore the relationship between biotechnology and other physico-chemical processes and to point out that biotechnology is but one of a portfolio of techniques for achieving clean industrial products and processes (see also Chapter 1), biotechnology is now so versatile that it is reasonable, when identifying the problems or bottlenecks to new developments, to seek biotechnological solutions.

◆ Figure 3.1. ***Clean technology, the drivers/stakeholders***



Source: R. Kurane.

BOTTLENECKS AND UNMET MARKET NEEDS

Impediments to the utilisation of biotechnology may be technical, when the scientific knowledge is insufficient, or sociological, when the attitudes of the public or industrialists need to change.

A number of issues have tended to limit the penetration of biotechnology for clean industrial processes. These issues, which include technical feasibility (Table 3.3) and demonstration of processes and products (Tables 3.4 and 3.5), form the basis for defining R&D needs. Identifying and overcoming these bottlenecks will lead to greater market penetration. Here, R&D is viewed from the perspective of market needs rather than technology push.

Among the technical impediments to the application of conventional biocatalysts to industrial processes are their hydrophilic nature and inactivation at high temperatures. In the petrochemical industry, most intermediates are water-insoluble, so that reactions currently need to be made in organic solvents. Additional technical problems associated with biological processes include high levels of water use, complex process equipment, and low yields due in part to incomplete understanding of metabolic pathways and physiological control mechanisms.

Another fundamental hurdle remains the lack of basic knowledge of microbial physiology, identified in the first OECD report on biotechnology (Bull *et al.*, 1982). While this is true of single species, it is even more so of bioconsortia. Relatively little is known about the interaction between micro-organisms and how, for example, the physiology of attached organisms differs from planktonic ones. Traditional biotechnologies are largely based on techniques for separating, growing, and analysing single species of organisms.

Commercially competitive use of the huge quantities of cellulosic, lignin and chitosan wastes generated by the agrifood and paper manufacturing industries is problematic because these wastes are more difficult to degrade than by-products such as whey and molasses. To make use of cellulose resources, searches have been made for micro-organisms with high cellulase activity, which could be used for new alcohol fermentations, for example. Similarly, research has been carried out on the microbial degradation of hemicellulose and chitosan, as a means of producing useful oligosaccharides. This exploitation of crop residues is usefully complemented by their use as feedstocks for value-added chemicals, such as organic acids and tetrahydrofuran.

Table 3.3. **Technical issues affecting the wider industrial application of biotechnology**

Industrial sector	Technical issues	Potential developments/solutions
Chemicals		
– Commodities	Reaction conditions (temperature, solvents)	Biodiversity (search and discovery) Protein engineering
– Plastics, polymers	Persistence Functionality	Biodegradable biopolymers Enzyme synthesis/modification
– Pharmaceuticals	Discovery rate Manufacturing costs	Bioinformatics Biodiversity/targeted screening Combinatorial chemistry/biochemistry Lead compounds based on non-natural substances
Pulp and paper	Lignin removal	Biobleaching Transgenic trees
	Waste recycling Chemical modification	Recycling of pulp “fines” By-product removal
Textiles and leather	Chemical texturing and dyeing Acid and alkaline processing conditions	Enzymes Extremophiles
Food and feed	Maintenance of sterile conditions	Thermophilic organisms Extremozymes
Metals and minerals	Metal toxicity Processing rates Waste management	Biodiversity Genetic manipulation
Energy	Low grade fossil fuels Recovery Sustainability Land requirement for biofuel feedstocks	Biodesulphurisation Enhanced oil recovery Hydrogen manufacture

Conventional industrial processes and materials, which have been developed over many decades, are perceived as having wide design flexibility. In part, this reflects the training and approach of chemical engineers and plant operators, whose familiarity with these processes has evolved slowly over the years. Biological processes and materials, on the other hand, may be perceived as lacking this flexibility. Biodegradable plastics, for example, currently lack the range of engineering properties of polymers derived from fossil fuels. However, biotechnology is now making it possible to synthesise novel polymers with specific regio- and stereoselective and other properties. Recent examples include linear polysaccharides and polyhydroxyalkanoate plastics, cyclodextrins, fluorescent polymers, and synthetic peptides containing man-made amino acids.

Table 3.4. **R&D efforts and bottlenecks to novel bioprocesses**

Process elements	Bottlenecks	Potential developments/solutions
Biocatalysis	Susceptibility to: organic solvents, heat, acids, alkalis, pressure, toxic hydrophilic substrates	Extremophiles, biodiversity search and discovery, biocatalyst immobilisation
	Catalytic properties: short half-life, too specific, chirality	Directed evolution, protein engineering, reaction conditions
	Multi-step reactions	Bioconsortium processes, pathway engineering
	Novelty: lack of biocatalytic analogues of chemical catalysts	Hybrid enzymes, ribozymes, abzymes
Bioprocess engineering	Monitoring/control	Biosensors, fuzzy logic control (artificial neural networks)
	Microaqueous systems	Membrane reactors
	High and low reactant concentrations	Process intensification, biocatalyst development
	Bioreactor design for animal and plant cell culture	Control of apoptosis, elicitation, signal transduction

Table 3.5. **Bottlenecks to the development of novel bioproducts**

Product innovations	Bottlenecks	Potential developments/solutions
Green commodities: biodegradable plastics, polymers, biofuels	Renewable resources, cheap fossil fuels, scale-up	Biomaterials and biofuels as alternatives to petrochemistry
Recycled products	Dilute organic wastes, recalcitrant wastes	Value-added products
Substitute products: microelectronic devices	R&D	Nanomachines
	Production scale-up	Biochips
Crop protection agents	Resistance, specificity and persistence	Biopesticides, plant growth enhancers
Biomaterials		
– Inorganic (magnetic, composite, complex architectures)	Natural resource depletion, bioprocess development	Biomimetics/biomolecular templates
– Organic (spider silks)	Factory farming	Fermentation technology, recombinant DNA technology

Bioprocess engineering: one example

At a stage in biotechnology development when innovation is dominated by molecular biology, there is a danger that bioprocess R&D will be neglected or insufficiently funded. Successful commercialisation of biotechnology is crucially reliant on bioprocessing engineering; Table 3.6 summarises some of the issues that must be addressed. For example, downstream processing, the separation and purification of post-culture products, is important for estimating the relative costs of industrial biocatalysts and chemical catalysts. Both direct monetary costs and environmental impacts must be taken into account, especially that of waste discharges on water quality. As an example, the production of biopolymers using micro-organisms typically requires five times as much water to separate the biopolymer from the biocatalyst than is required for conventional chemical processes. This means the need for more energy and much higher water processing capacity and thus an environmental impact that goes well beyond simple cost considerations. One approach to resolving this type of problem may be to conduct the synthesis in two-phase water-organic solvent systems with recycling of the organic component.

Integrated bioprocessing is a timely development in this context. It attempts to integrate enhanced biocatalyst activity and procedures for partitioning the catalysts and the reactants (substrates, products) and effecting some measure of purification, *i.e.* simplification of the overall process by reducing the number of separate unit stages. An interesting recent example of integrated bioprocessing is the simultaneous saccharification and extractive fermentation reported by Moritz and Duff (1996). Cellulose

Table 3.6. **Large-scale bioprocess engineering issues**

Low efficiency and high costs of bioprocessing
Low product yields
High water consumption
Strain instability and metabolic variability
Development of bioconsortia-based processes
Risk of contamination caused by processing at ambient temperatures
Downstream processing: separation, purification for integrated bioprocessing
Bioreactor innovation for microbes; monitoring/control
Expensive equipment owing to the complexity of processes
Need for operators with different skills
Lack of on-line monitoring and control
Problems peculiar to recombinant products (*e.g.* authenticity of post-translational processing of proteins) (see Case Study 3.1, page 81)
Plant and animal cell culture technology

feedstock is hydrolysed by enzymes to glucose, which is then removed by fermentation to ethanol by yeast in order to prevent feedback inhibition of the cellulose hydrolysis. Ethanol, in turn, depresses the fermentation rate and is extracted by the biocompatible water-immiscible solvent, oleyl alcohol. All these reactions take place in a single reactor vessel rather than as multiple unit stages each requiring its own processing equipment. Particularly encouraging is the application of partitioning bioreactors for synthesising and recovering high-value products, including proteins.

Many new bioreactor designs are now available which may accommodate novel biocatalytic reactions. There remains, however, the inevitable question of scale. Fine chemicals and pharmaceuticals are often produced using biocatalysis on relatively small scales. Some commodity chemicals and foods can be produced on a large scale using biocatalysis. Thus, there is a broad range of applications of biotechnological processes which can be employed for industrial production. Demonstration projects are critical for establishing that laboratory and small-scale R&D activities can be scaled to needed industrial production levels for specific applications.

OPPORTUNITIES

Opportunities for developing and implementing clean or cleaner biotechnology arise from the fact that many current products and processes are now regarded as environmentally unfriendly, and many are major sources of pollution. Biotechnology may well be able to provide clean or at least less polluting alternatives to existing practices that generate environmental problems, as other parts of the report make clear. The challenge to biotechnology now is to improve environmentally sensitive industrial operations and manufactures (for examples, see Table 3.7). What problems might be amenable to biotechnological intervention, either for remediation or for provision of novel clean alternatives?

Box 3.1. **Biohydrogen**

Hydrogen gas has often been cited as the ultimate clean fuel: energy is released by burning it, and the only product of combustion is water – no carbon dioxide is released. Micro-organisms have long been known to be prodigious hydrogen gas producers, and thus the question has been raised as to whether it makes economic sense to attempt to produce hydrogen gas for fuel via biotechnology.

Anaerobic bacteria are the main agents of hydrogen production in nature, and two different sorts of enzyme systems have been described that produce hydrogen gas: hydrogenases and nitrogenases. Under anaerobic conditions, bacteria often get rid of excess electrons by hydrogenase-catalysed reduction of protons to hydrogen gas. However, in terms of energy, this process is slightly unfavourable, and, in nature, only relatively small amounts of hydrogen are usually released via this mechanism. Nitrogenases, on the other hand, are responsible for much larger amounts of hydrogen production, even though the primary function of those enzymes is believed to be nitrogen fixation. It appears that one molecule of hydrogen is produced for each molecule of nitrogen that is fixed.

Of special interest to biotechnologists are the photosynthetic nitrogen-fixing bacteria, which can use solar energy to drive the production of hydrogen. Some of these organisms obtain the required electrons from organic waste, while others are capable of splitting water. Each system is currently being examined, especially in European and Japanese laboratories, in attempts to combine biotechnology and engineering in ways that will produce useably pure hydrogen at low cost. Each has many challenges to overcome before it can compete with physical and chemical sources of hydrogen.

It is important to keep in mind: *i)* that many petrochemical processes are catalytic and produce high yields of desired products; and *ii)* that to describe processes as inherently environmentally sensitive may be misleading (the hydrogen cyanide by-product from acrylonitrile synthesis, see

Table 3.7. **Environmentally sensitive processes and products**

Process or product	Environmental problem
Organic chemical syntheses	Acid and solvent emissions; residues
Aromatic amines	Iron in process water
Acrylonitrile synthesis	Hydrocyanic acid emission
PETP synthesis	Methyl ester accumulation
Glycol ether scrubbing of pharmaceuticals' waste gases	Inability to separate the resulting solvent mixtures
Agrichemicals	Dispersion; eutrophication
Inks, varnishes, adhesives	Solvent emissions
Synthetic plastics and detergents	Persistence

Source: Wiesner, 1995.

Table 3.7, is used, for example, to make acetonitrile or methylmethacrylate). Thus, the identification of priority targets for biotechnology cannot be made on simplistic criteria. Instead, holistic analysis of processes is essential.

Industrially sustainable products and processes

Many widely used synthetic organic compounds have great economic importance for a range of applications, yet have adverse effects on the environment and human health. The development of novel substances that will minimise environmental and health risks are therefore both urgently needed and attracting considerable research interest. Strategies incorporating a "green design principle", which addresses each step in the production, use, and ultimate disposal of an environmentally friendly product, will be important for reducing adverse environmental impacts (see also Chapter 4). Design for Environment is one means of achieving this objective (Box 3.2).

Box 3.2. **Design for Environment (DFE)**

DFE seeks to ensure that all relevant and ascertainable environmental considerations are integrated into product or process design. The goal is to achieve environmentally friendly manufacturing products and processes while maintaining competitive price and performance. DFE can be implemented in the course of an entirely new industrial development; equally importantly, it can be incorporated into existing operations and consequently reduce the cultural shock and high capital costs that are likely to be involved in replacing inherently "dirty" by new "clean" technology. In this context, a discipline is imposed on DFE that ensures its practicality in a commercial operation. DFE emphasises the need for a holistic approach to environmental protection in a high-technology economy: it incorporates concepts such as reduced use of toxic materials, waste minimisation, design for recyclability, and many others, in a complex multidimensional analysis. Life Cycle Assessment (LCA) (see Chapter 4) complements DFE by generating environmental impact data; LCA *per se* does not provide a mechanism by which identified environmental considerations are incorporated into green product and process design. Green design can help manufacturers generate less waste and reduce production costs at the same time. As waste disposal costs and regulatory compliance penalties increase, the environmental attributes of products will necessarily become more important to consumers and investors. All of these trends suggest that having an environmental dimension in a company's strategy will be an increasingly essential competitive asset.

Source: Allenby, 1994.

This design principle can be illustrated by reference to the "greening" of an existing process, *e.g.* the development of a novel flocculating agent. Case Study 3.2 (page 82) describes the integration of a biotechnology stage into existing manufacturing plants that use chemicals to impart wet strength to paper and cellulosic packaging materials, and which, as a result of the chemistry employed, generate unwanted organochlorine by-products.

High polymer flocculating agents, polyacrylamide derivatives in particular, are frequently used in a wide range of applications, including wastewater treatment. Many consumer products requiring water absorbency also are fabricated from high polymer materials such as polyacrylate and polyacrylamide derivatives. These synthetic polymers are both cost-effective and performance-effective. In passing, it is interesting to note that biotechnology has delivered an environmentally benign route to acrylamide from acrylonitrile based on immobilised bacteria, with current annual production of over 10^4 tonnes. Unfortunately, there are environmental problems associated with both the polymers (poor biodegradability and hence persistence) and the acrylamide monomer (toxicity).

Kurane *et al.* (1994) have explored possibilities for producing novel bioflocculants and have discovered a protein that efficiently flocculates organic and inorganic particulate materials ranging from activated sludge to power station fly-ash and environmentally damaging water-soluble pigments. Feasibility studies on this flocculant have demonstrated its effectiveness in coping with waste streams arising from domestic livestock, pulping, and the pharmaceutical and food processing industries.

Biotechnology for the chemicals industry

The enormous annual production of chemicals world-wide indicates the extent to which society depends upon them. This output represents not only consumer products but vital chemical feedstocks and materials for other industries as diverse as food, pharmaceuticals, energy, telecommunications, and leisure. The choice of the chemical industry as an example is therefore a logical and appropriate one, but similar considerations apply to all industrial sectors.

Chemical processes are often conducted at high temperatures and high pressures. They therefore not only consume large quantities of energy but also generate residues and by-products that must be removed from the desired product. There are various ways to minimise or prevent the generation of by-products, such as designing new synthesis routes, developing improved catalysts, improving catalyst selectivity, and changing the reaction medium. All these options are open to biotechnology. Case Study 3.3 (page 83), for example, demonstrates the superiority of a new enzyme-based route to 7-aminocephalosporanic acid (7-ACS, the starting point for semisynthetic cephalosporin antibiotics) in reducing residues and the use of environmentally sensitive auxiliary materials.

Improved and novel biocatalysts

The development of novel catalysts focuses on three approaches: *i)* search in natural habitats, such as geothermal sites, for biocatalysts that can function at high temperatures and in artificial environments; *ii)* modification of existing biocatalysts by genetic or physico-chemical methods; and *iii)* design of catalysts from organic or inorganic molecules (see Annex 1.2). Natural biocatalysts comprise enzymes that may be cell-free or contained within viable or non-viable micro-organisms or other cells.

With the recognition that less than 1 per cent of the micro-organisms in nature have been cultured, the search is on to examine the as yet unexplored microbial biodiversity. A wealth of biocatalytic potential presumably remains untapped. Through bioprospecting, much of this naturally occurring potential may be discovered and developed for industrial applications.

Several new developments in molecular biology are facilitating this exploration of the microbial world and helping to capitalise on its genetic potential. Gene probes are being used to identify micro-organisms in natural samples on the basis of their taxonomic or functional properties. In this manner, micro-organisms with specific biocatalytic properties can be detected even when they are not yet culturable. When such organisms are identified, efforts can be directed at their cultivation and industrial exploitation.

Genomic studies are also revealing the sequences and functions of genes. This information can be used to design new gene probes for detecting organisms with related but novel enzymatic capabilities. Thus, one can now rationally design screening programmes for recovering biocatalysts, which can then be selected for their ability to function in clean industrial processes.

Biocatalysts effect a great variety of chemical reactions with high specificity, but catalytic rates are susceptible to a variety of denaturing agents and conditions (metals, solvents, heat), and frequently have rather short operating half-lives. However, over the past few decades, considerable progress has been made in improving the catalytic stability of enzymes and cells; more recently, research has focused on improvements directed at modifying substrate specificities, functioning in a non-aqueous milieu, and the efficiency of enzyme production. Glucose-6-phosphate dehydrogenase (G6PDH) is a thoroughly analysed case of enzyme over-production which also demonstrates the power of recombinant DNA technology to reduce pollution. The enzyme was produced initially in low yield by the bacterium *Leuconostoc*. Cloning of the G6PDH gene into *Escherichia coli* ultimately led to a 1 000-fold increase in production for a comparable fermentation volume. The recombinant *E. coli* process resulted in very large savings in raw materials and energy and in the pollution load of the process. Table 3.8 shows the dramatic effects that improving enzyme productivity has on pollution prevention.

Table 3.8. **Pollution reduction using a recombinant bacterium in biocatalyst production**

Process component	*Leuconostoc*	Recombinant *E. coli*
Fermentation volume (m^3)	600	1
Growth medium constituents (kg)	64 000	160
Bacterial mass (kg)	22 000	200
Process water (m^3)	10 260	71
Cooling water (m^3)	15 000	30
Air (m^3)	114 000	570
Electricity (kWh)	20 000	370
Steam (t)	180	10
Ammonium sulphate (kg)	13 000	200
Wastewater (m^3)	1 200	0.2
Pollution load (PE)	300 000	300

The pollution load (PE) is equivalent to one person per 24 h.
Source: Wiesner, 1995.

The most exciting events in biocatalysis in recent years have been the development of catalytic molecules to bring about unnatural reactions and the on-going search for novel enzymes in nature. As Zhang *et al.* (1997) have stated, "Proteins and enzymes with novel functions and properties can be obtained either by searching the largely unknown natural species or by improving upon currently known natural proteins or enzymes. The latter approach may be more suitable for creating properties for which natural evolutionary processes are unlikely to have been selected." Much of the impetus for researching extremophiles (micro-organisms that grow optimally at extremes of temperature, acidity, alkalinity, pressure, salinity, aridity, radiation dosage, etc.) has been the expectation that their enzymes may show optimum catalysis under conditions that would be desirable for industrial or domestic processing. Enzymes that fall into this category have been termed extremozymes and several have been commercialised (see Chapter 2). The discovery of extremophiles and other novel microbial diversity has become a sophisticated activity based on microbial ecology and oligonucleotide probing of environmental samples. The detection of novel extremozymes can be exploited in a comparable way by cloning random fragments of DNA recovered from environmental samples and screening the resultant clones for activities of interest.

Box 3.3. **Directed evolution of enzymes**

Chemical engineers who try to design real industrial processes using biological catalysts are constantly stymied by a simple fact: biological systems have evolved over billions of years to perform very specific reactions within specified environments. Some of the features required for functioning in a complex chemical network are undesirable when the catalyst is removed from its natural context. Conversely, many of the properties we wish an enzyme would possess clash with those desired for industrial processes. Recently, directed evolution has emerged as a powerful alternative to rational protein engineering for the development of novel enzymes.

Directed evolution is a very practical approach for tailoring enzymes for a wide range of applications. By building them with new features and functions, enzymes can be "tuned" to function optimally under specified conditions. Mimicking key processes of Darwinian evolution in the test tube makes it possible to explore the functions of enzymes free from the constraints of function within a living system. Moreover, directed evolution can be applied even when very little is known about an enzyme's structure or catalytic mechanism. Since the vast majority of proteins remain largely uncharacterised, this marks a huge advantage for the method. Because this approach allows for exploring novel solutions to protein design problems, it also promises to reveal a great deal about protein structure and function. It has been used to effect improvements in enzyme stability (melting temperature, catalytic half-life, stability in organic media), substrate specificity, and enantioselectivity (selection of one-handed molecules).

The protease enzyme subtilisin, which is used as a laundry aid, is stabilised by calcium. Unfortunately, industrial use of this enzyme frequently occurs in the presence of metal-chelating chemicals. As a result, calcium is removed and the enzyme is destabilised. The amino acid sequence of the enzyme that binds calcium can be deleted, and directed mutagensis and selection can then be used to evolve subtilisin stability, which is independent of calcium. An evolved enzyme has been produced that retains the native catalytic activity but has a 1 000-fold increased stability under strong chelating conditions.

Bacterial esterase has been evolved to replace a zinc-solvent procedure involved in the production of semi-synthetic cephalosporin antibiotics. Sequential mutagenesis and a random gene recombination of positive variants created a new enzyme with a 50-60-fold enhancement of activity over the native enzyme. This shows the possibility of developing a more environmentally friendly process by sparing the use of solvent and preventing zinc-containing waste.

Future research in directed evolution will include development of large-scale screening methods, so as to allow efficient searches of large mutant libraries. The construction of optimised mutant libraries will also decrease the need for screening. In addition to streamlining efforts to "tune" enzymes, these improvements will allow larger leaps, such as the evolution of new catalytic activities. Significant improvements in the ease and power of directed evolution will also come from the optimising of the search strategies. The many similarities to optimisation problems in other fields make this a fertile ground for collaborative efforts among theoreticians and experimentalists from a wide range of engineering disciplines.

DNA shuffling has recently been developed to evolve a fucosidase activity from a bacterial galactosidase. After seven rounds of DNA shuffling and screening, an evolved enzyme was recovered which showed a 1 000-fold increase in fucosidase specificity compared to the native enzyme. DNA shuffling also can be used to combine two or more properties that have been evolved separately. Directed evolution of subtilisin, for example, has produced variant enzymes with either improved stability towards hydrogen peroxide, or with enhanced activity; variants rarely showed improvements in both properties. However, the two variant populations can be recombined to create enzymes that are more stable and more catalytically active.

Source: Stransberg *et al.*, 1995; Moore and Arnold, 1996; Arnold, 1996; Zhang *et al.*, 1997; Kuchner and Arnold, 1997.

Over the past decade, the range of biocatalysts has widened to include catalytic RNA (ribozymes) and catalytic antibodies (abzymes), and artificial analogues of some of these molecules have also been created. In general, ribozymes are not as catalytically efficient as proteins, but they are capable of effecting complex transformations, and the development of novel artificial ribozymes is extending significantly their catalytic repertoire. One of the latest breakthroughs in this field has been the building of a regulatory mechanism into ribozymes which mimics the control exerted over many protein enzymes. An ATP-binding site was stitched to a ribozyme to create for the first time an allosteric ribozyme: in allosteric control, a binding site can specifically recognise certain small molecules and alter the catalytic rate by changing the conformation of the protein, and now, the RNA. In this case, the presence of ATP activates the ribozyme. One realisable goal is to couple a catalytic function to a molecular switch, an achievement that could offer the prospect of RNA-based networking systems, analogous to artificial intelligence.

Catalytic antibodies (abzymes) were first reported just over a decade ago. The compelling attraction of antibodies is their extraordinarily high specificity, which means that a specific antibody can be raised, at least potentially, against any substance. In other words, the immune system provides the opportunity for creating tailor-made catalysts. The technology of abzyme production is beyond the scope of this report, but types are now available that can catalyse a wide range of chemical reactions. There is a wide variety of potential applications for abzymes, from difficult-to-treat drug addictions such as cocaine to the catalysis of chemically unfavourable reactions.

Despite intense research into fundamental features governing protein folding and function, there are enormous gaps in our understanding of two critical processes: the relationship between sequence and structure and the relationship between structure and function. As a result, the rational design of new proteins via the classical reductionist approach has been a frustrating exercise (Arnold, 1996). A recently designed strategy in which the properties of natural enzymes or proteins are modified in order to create desirable properties has become known as "directed evolution" (Box 3.3). It involves creating sequential rounds of mutagenesis in order to produce a library of mutants which can be screened; the mutants selected in each round become the parents for the next round. Mutants can be generated in various ways to produce random or site-directed changes in the DNA, and the mutation frequency can be optimised to accommodate the constraints of the screening programme. A complementary approach is the technique of "DNA shuffling", which involves taking a set of closely related DNA sequences, fragmenting them randomly, and reassembling the fragments into genes. This process rapidly produces a combination of positive (desired) mutations as the output of one cycle becomes the input for the next cycle and reiterative DNA shuffling leads to effective directed evolution. A great advantage of these procedures is that they can be applied to evolve any protein rapidly even if the structure is unknown.

The environment for biocatalyst reactions

The use of organic solvents to enhance the biotransformation of poorly water-soluble compounds is now well established in R&D. Also, micro-organisms are being discovered that can grow in remarkably high concentrations of solvents (*e.g.* 50 per cent v/v toluene), or can be evolved to develop such capabilities (see Box 3.4). Attention has turned more recently to supercritical fluids (SCF) as media for biocatalytic reactions (Kamat *et al.*, 1995). Supercritical fluids are non-aqueous materials held above their critical temperature so that they cannot be liquefied; they bridge the gap between the properties of liquids and gases. SCFs offer a number of major advantages for bioprocessing, including the solubilising of hydrophobic reactants, low toxicity, increased enzyme reaction rates, ease of downstream operations, protection against microbial contamination, and options for recycling. Evidence is accumulating that enzyme activity, substrate specificity, and enantioselectivity (selection of one-handed molecules) all can be manipulated by modifying the pressure under which the reaction is made. For example, lipase from the yeast *Candida* will catalyse a reaction between methylmethacrylate and ethylhexanol to produce chiral polymers; the reaction rates are significantly increased when the reaction occurs in SCFs such as sulphur hexafluoride. Lipase has also been used to catalyse polyester synthesis, and, when the reaction is carried out in SCFs such as fluoroform, the molecular weight of the polymer can be controlled by the reaction pressure.

Box 3.4. **Non-aqueous biocatalysis**

A relatively recent finding of significance for clean industrial processes is that enzymes can retain their catalytic activities in the absence of water. Biocatalysts in non-aqueous media can be used in various industrial processes where the introduction of water is undesirable. The phenomenon of enzymatic catalysis in organic solvents appears to be due to the structural rigidity of proteins in organic solvents that results in barriers to their unfolding. Applications of bioprocessing in non-aqueous media are expected to provide significant advances in the areas of fossil fuels, renewable feedstocks, organic synthesis, and environmental control technology.

Solid enzymes exposed to non-aqueous solvents exhibit remarkable novel properties, *e.g.* greatly increased thermal stability and strikingly different substrate specificities. Consequently, a number of interesting and useful enzymatic conversions can be accomplished in organic solvents. In order to take advantage of the novel opportunities offered by non-aqueous biocatalysis, it is imperative to understand the basic features and characteristics of the influence of the solvent on the enzyme and its catalytic properties. A detailed understanding of environment/structure/function relationships for enzymes suspended in organic media may enable predictive control of enzyme functions merely by manipulating the solvent.

Supercritical fluids represent a unique class of non-aqueous media for biocatalysis. The inherent gas-like low viscosities and high diffusivities of SCFs increase the rates of mass transfer of substrates to the enzyme. Conversely, their liquid-like densities result in higher solubilising power. The physical properties of an SCF can be adjusted over a wide range by a relatively small change in pressure or temperature. The advantages for using enzymes in SCFs include: synthesis reactions in which water is a product can be driven to completion; the solubility of hydrophobic materials is increased; the thermostability of biomolecules in supercritical fluids is greater than in water; the solvent can be readily recycled; biochemical reactions and separations can be integrated into a single step.

Source: Zaks and Klibanov, 1988; Kamat *et al.*, 1995.

EMERGING TECHNOLOGIES

The biocatalysis discussed above concerns relatively simple, single-step reactions. Traditionally, fermentation processes based on defined monospecies have been the route for producing complex, multi-step syntheses and chemical transformations. Complementary genetic capabilities are also being used to achieve greater processing versatility and to create metabolic opportunities that have not evolved in natural organisms. These approaches are embodied in mixed microbial cultures (bioconsortia), genetic engineering to create recombinant organisms, and metabolic pathway engineering.

Bioconsortia

The empirical discovery and exploitation of bioconsortia has ancient antecedents, but the drive to identify the causal agents of human and other animal diseases in the 19th century inevitably led to a long period of so-called pure culture microbiology. With a few notable exceptions, such as the activated sludge process for sewage treatment introduced in 1914, the Koch tradition of monospecies cultivation has dominated 20th century microbiology, and hence biotechnology. A notable recent exception is a polysaccharide bioflocculant, a substance produced by a mixed culture of micro-organisms (Kurane and Matsuyama, 1994). There has nonetheless been a resurgence of interest in bioconsortia following the emergence of a widespread wish to produce microbial protein from renewable resources, or from natural gas (or methanol). Despite excellent research and process development, these bioconsortium-based activities have not met with commercial success, largely because they were unable to compete with soya protein. Since the early review of bioconsortium microbiology and biotechnology (Bull and Slater, 1982), bioconsortium research has continued rather spasmodically in areas such as toxic waste treatment, metal accumulation, steroid transformations and, ironically, pathogenicity. Interest in bioconsortia also has returned in the context of developing integrated bioprocessing (see the section, "Bottlenecks and unmet market needs", above).

The merits of using bioconsortia in industry are recognised. They include increased yield of product, reduced risk of contamination (see Case Study 3.3, for examples), increased resistance to process perturbations, and, in certain cases, reduced effluent load. Bioconsortia can be of two types: mixed populations of natural micro-organisms, the composition of which is often undefined; and constructed populations of defined micro-organisms. When developing biotechnological processes with natural consortia, it is important for several reasons to identify the composition of the mixed population. The process should operate with organisms "generally regarded as safe", and unknown members of a consortium may not meet this requirement. In addition, process control and stability may be compromised if all the component organisms are not recognised and their function in the consortium goes undetected. The association of different species may be so intimate that a mixed population may pass unsuspected. For example, in 1940, *Methanobacillus omelianskii* was identified as a single, methane-producing species, and only 27 years later was it discovered that this was an association of two distinct species whose metabolic integration was extremely tight and essential for the production of methane.

Recent cultivation-independent techniques such as fluorescent *in situ* hybridisation (FISH) is making it possible to resolve the structure and dynamics of even the most complex bioconsortia. Signatures of micro-organisms reside in the sequence of nucleotides in their ribosomal RNA. Oligonucleotides that are complementary to these signatures can be designed and, when attached to fluorescent labels, be used to detect specific micro-organisms within bioconsortia. One of the most dramatic applications of FISH has been for the analysis of the activated sludge bioconsortium, which was presumed well-known. Based on traditional cultivation protocols, it was believed that the dominant bacteria in activated sludge were Proteobacteria of the gamma sub-class. Application of FISH proved that this assumption was erroneous, and that bacteria of the beta sub-class were in fact most abundant *in situ;* it showed, in other words, that conventional plating methods are unreliable. A pressing need for biotechnology research, therefore, is to develop new procedures to culture the organisms that are dominant in ecosystems and can be detected but as yet have resisted cultivation in the laboratory. The combination of FISH with the use of microsensors to analyse both community structure and function at the scale of individual micro-organisms should increase significantly the understanding of bioconsortium behaviour.

Bacteria have evolved a variety of biochemical transduction mechanisms for recognising signals in their environment and thereby controlling their gene expression. While the sensing of information from the physico-chemical environment and from animals and plants has been extensively documented, the dramatic nature of signal transmission among bacteria has only recently come to light. Of particular interest are the communication mechanisms that bacteria have evolved to sense their own population densities and to regulate their gene expression accordingly. According to Gray (1997), "Before any form of bacterial group response is initiated, the density of the population must be assessed: how many cells are available to divide the necessary labor or to join the unified mob?" Quorum sensing (Box 3.5) is one of the most widespread mechanisms among bacteria for communication and triggering co-operative behaviour.

The signal molecules in Gram-negative bacteria are lactones (so-called autoinducers), while many Gram-positive bacteria produce peptide signals (so-called pheromones) that have quorum sensing functions. Within these broad groups of bacteria, it is entirely possible that interspecies communication takes place and that one species may change its behaviour in response to the presence of others. Knowledge of such interaction could be crucial for understanding the overall behaviour of bioconsortia and how it might be manipulated for biotechnological purposes. The concentration of signalling molecules will increase as populations increase and under circumstances where the diffusion away is restricted, as may be the case in biofilms and other aggregations of micro-organisms. Therefore, the quorum sensing phenomenon should now be kept in mind when analysing and designing bioreactor systems based on attached cells.

Box 3.5. **Quorum sensing**

Like ants, bacteria appear to be social organisms. Until a few years ago, it was thought that signalling in microbial systems was a very limited evolutionary event. It had been documented in slime moulds, myxobacteria and the actinomycete *Streptomyces* but little else. These isolated cases are now seen as the tip of an iceberg in microbial sociability.

The benchmark for modern studies of microbial signalling and population response is bioluminescence in the marine bacterium *Photobacterium fischeri*. In the simplest terms, a gene, *lux*I, encodes for the synthesis of a member of a class of quorum sensing compounds, the N-acyl homoserine lactones (AHLs). A second gene, *lux*R, encodes for a protein that activates *lux*I in response to the presence of an AHL. Thus, the overall effect, when the AHL reaches a threshold concentration, is a rapid amplification of the inducing signal. In *P. fischeri* and other Gram-negative bacteria, the homoserine lactone signal molecules need to be inside the bacterium to elicit their effects.

Gram-positive bacteria have not been reported to produce homoserine lactone signals; instead, the common signal molecules are peptide pheromones (PP). The PP is recognised by a sensor component of a two-component regulatory system; again, the synthesis of the PP is an autoregulatory process which triggers PP synthesis and population-density-dependent behaviour. In contrast to the homoserine lactone signals of Gram-negative bacteria, PP interact with sensing proteins on the surface of the cell membrane and do not need to penetrate the cell.

The range of population-density-dependent behaviour includes luminescence, swarming motility, cell division, and the synthesis of virulence factors, secondary metabolites (antibiotics, pigments), polysaccharides, and enzymes in Gram-negative bacteria, and genetic competence and the synthesis of virulence factors and antibiotics in Gram-positive bacteria. One intriguing aspect of this area of research might be the ability to block pathogenesis by disruption of quorum sensing in disease-causing bacteria. Thus, the development of AHL antagonists offers the possibility of new therapeutic compounds for controlling infections. From the biotechnology perspective, a particularly exciting property of AHLs and AHL analogues is their ability to effect alloinduction and/or alloinhibition. Alloinduction is the phenomenon of gene activation in one species by another species, while alloinhibition describes the incapacitation of one species caused by a signal from another organism. Alloinduction can be used as a search and discovery stratagem for natural products by challenging micro-organisms with AHLs and screening for the products of silent genes. The production of carbapenem antibiotics by the plant pathogenic bacterium *Erwinia caratovora* in response to N-(3-oxohexanoyl)-L-homoserine lactone is an example of such discovery.

Source: Fuqua *et al.*, 1996; Gray, 1997; Robson *et al.*, 1997; Kleerebezem *et al.*, 1997.

There is another feature of quorum sensing that has biotechnological possibilities, namely communication between different species of bacteria. It is known that a large number of species produce autoinducers, or pheromones, and that the ability of species to distinguish between different signal chemicals is not absolute. Moreover, it is now relatively straightforward to screen for signal production, and libraries of these chemicals can be expected to be built up in the near future. It may be feasible, therefore, to use autoinducers and pheromones to elicit metabolic activities and compounds (*e.g.* antimicrobials, receptor antagonists, enzymes) that can be entered into high throughput screens and thus extend the options for biotechnology search and discovery programmes.

Recombinant DNA technology

Recombinant DNA technology provides a very powerful method for combining diverse genetic capabilities. It permits the genetic engineering of organisms with specific catalytic capabilities. Thus, organisms can be engineered to carry out specific catalytic activities and to function at high temperatures, at high solvent concentrations, or other conditions that characterise industrial processes. In many cases, enzymes from organisms that grow naturally in extreme environments, such as hot springs or deep sea thermal vents, are sought. These enzymes can then be transferred into more manageable organisms such as *E. coli* or yeasts that are traditionally cultured in industrial reactors. Conversely, the catalytic capabilities of less tolerant organisms can be transferred to those that grow best under harsh environmental conditions.

Recombinant organisms can be used to produce enzymes that are useful biocatalysts (see Table 2.9). Since these recombinant organisms can be grown under contained good large-scale industrial practices, safety issues relating to environmental release are minimised. There are advantages to using the recombinant enzymes but some countries, such as Germany, still require the use of the non-recombinants for certain applications, such as food production.

Modern biotechnology can have a favourable environmental impact compared with traditional techniques (see also Chapter 1). For example, enzymes derived from recombinant organisms have higher fermentation yields and therefore reduce the consumption of resources for their production. Table 3.9 compares resource consumption for making a given enzyme using conventional and genetically modified organisms. The figures give an index for consumption per metric tonne of enzyme produced based on the conventional production organism.

Table 3.9. **Reduced consumption of resources from genetic engineering**

	Raw materials (weight)	Water (weight)	Steam (weight)	Electricity (kWh)
Conventional micro-organism				
Fermentation	65	36	26	75
Recovery	35	64	74	25
Total	100	100	100	100
Genetically modified micro-organism				
Fermentation	32	18	13	38
Recovery	27	35	39	13
Total	59	53	52	51
Percentage saved	41%	47%	48%	49%

Source: Novo Nordisk, 1996.

Another example of how cleaner enzyme production can be achieved by replacing traditional fermentation processes by modern biotechnological fermentation is described in Table 3.8.

Many biotechnological applications for cleaner industrial products and processes will rely upon recombinant micro-organisms. Most of the processes will be contained and hence subject to existing guidelines for industrial applications of recombinant DNA. Under the OECD criteria for industrial applications of recombinant DNA, organisms should be handled under conditions of good industrial large-scale practice (GILSP) (OECD, 1986). GILSP requires appropriate containment that is commensurate with the risk presented by the recombinant organism. Containment may be achieved biologically, on the basis of inherent properties of the organisms which limit their survival in the environment and their ability to transfer DNA to other organisms; or physically, on the basis of equipment, operating practices, and facility design which minimise potential releases of the recombinant organisms to the environment. The degree of physical containment should match the risk presented by the organism. This approach to the handling of recombinant organisms should be applicable to clean industrial processes in most cases and should be able to rely upon the existing safety practices that are used to manage other organisms.

With regard to cleaner products achieved through biotechnology, the scientific consensus is that risk should be assessed on the basis of the inherent properties of the product rather than the process used for its manufacture. Accordingly, the same considerations apply to products made by recombinant organisms and those made by other means. It is appropriate, however, to examine possible contamination of the product with recombinant DNA or any other substances used in its production. Thus, it may be appropriate, for products formed using recombinant organisms, to consider whether the introduced recombinant DNA, or any other substances used in their production, require special scrutiny as possible sources of contamination. In some countries, there is additional regulatory oversight for any processes that employ intergeneric recombinant organisms for commercial purposes, including R&D as well as actual production. Generally, the degree of regulatory restrictiveness is greatly reduced when the process is well contained and as long as it follows good industrial large-scale practice.

Metabolic pathway engineering

The establishment of mixed microbial cultures is one way of combining different, complementary metabolisms in order to bring about desired transformations and syntheses. An alternative strategy now attracting much interest is pathway engineering, *i.e.* the assembly, via recombinant DNA technology, of metabolic sequences in a single organism. Early targets in this context were the design of micro-organisms to effect the degradation of toxic environmental chemicals. Chemicals such as polychlorinated biphenyls, dioxins, and chlorodibenzofurans are very recalcitrant and few organisms, if any, have been isolated that can, on their own, degrade or detoxify them effectively. The construction of genetically engineered bacteria able to metabolise chemicals of these types has been achieved by recruiting enzymes from different organisms with complementary activities. Recently, DNA shuffling (see Box 3.3) has been successfully deployed for the first time for the evolution of a metabolic pathway *in vitro,* namely, a 3-gene operon coding for resistance to arsenic (Crameri *et al.,* 1997).

With regard to biosynthetic pathways, the fermentation industry has considerable experience with feeding so-called precursor chemicals to microbial cultures, with a view to their incorporation into target products, such as antibiotics, as a means of generating novelty. A contemporary illustration of this strategy is the production of novel erythromycin antibiotics in a two-stage bioprocess. In the first stage, normal antibiotic precursor synthesis was prevented; it was replaced by feeding artificial analogues to the culture. The resulting unnatural intermediate compounds were then metabolised further in the second stage by another bacterium, resulting in the production of novel antibiotics. The logical extension of such experiments is to use recombinant DNA technology to assemble the novel biosynthetic pathway *in vivo* in a single organism.

The best examples of pathway engineering are in the field of aromatic polyketide biosynthesis where, as a result of mixing and matching appropriate enzymes, hybrid biosynthetic pathways have been created. Polyketides comprise a large family of natural products found in bacteria, fungi, microalgae and plants; they include commercially important bacterial products such as antibiotics (erythromycin, tetracycline), antiparasitics (avermectin), anticancer (doxorubicin) and immunosuppressant (rapamycin) compounds. The biochemistry and genetics of certain polyketide syntheses are known in great detail, particularly in *Streptomyces* bacteria, where the cluster of genes that control polyketide synthesis have been extensively characterised. These genes code for modular arrays of biosynthetic enzymes (the so-called polyketide synthase enzymes, PKSs), and PKSs from different bacteria can be genetically recombined to yield novel compounds. Initially, these constructions were made empirically, but, as the individual enzymes have been better understood, rules for rational design of novel polyketides have been established. Four enzyme activities constitute the minimal PKS necessary to synthesise a polyketide; various auxiliary components of the PKSs catalyse modifications of the basic structure which may alter its size and shape and hence its biological activity. Thus, as Hopwood and Khosla, the two main proponents of this strategy, state, "the potential for generating molecular diversity within this class of molecules is enormous" (McDaniel *et al.,* 1995). The next phase of this research almost certainly will include some form of directed evolution of PKSs to create catalytic properties not found in the natural enzymes and thereby increase even further the opportunities for novel polyketide designs.

Research is also progressing on the development of so-called "one-pot" multi-enzyme reactors for achieving complex syntheses. Here, mixtures of enzymes are used in cell-free systems; among the successes to date has been the *in vitro* synthesis of a natural polyketide, tetracenomycin, from simple fatty acid substrates. As more natural and mutant PKS enzymes become available, the possibility of producing novel polyketides *in vitro* will follow.

BIOINFORMATICS

Bioinformatics is a new interdisciplinary field, with its basis in computer science, mathematics, computer and software engineering, and biology. It is concerned with the assembly, storage, retrieval and analysis of computer-stored databases (Benton, 1996). The databases include DNA, RNA and protein sequences, macromolecular structure information, and a large number of specialist databases that include phenotypic information. Among the latter can be found taxonomic information, metabolic pathways, and two-dimensional gel electrophoresis profiles of cellular proteins that are the basis of proteomics (see below). The goal of genomic research is to obtain gene maps and the complete DNA sequences of organisms; this was first achieved in 1995 for two bacterial species. Four more microbial genome sequences were announced in 1996, and by the end of the century, tens of sequences are expected to be available. In addition, mapping and sequence analysis of various animal and plant species are also proceeding rapidly. One of the projects is the human genome.

Data from genomic analyses can be used to address a variety of questions related to the pathogenicity of micro-organisms, the genetic basis of human disease, molecular evolution, and the biotechnological exploitation of novel organisms such as extremophiles. For example, it is estimated that as much as half of the world's population carries the bacterium *Helicobacter pylori*, which can cause peptic ulcers in humans. The recent publication of the *Helicobacter* DNA sequence (over 1.6 million nucleotide base pairs) will provide new insights into its pathogenicity and greatly aid the pharmaceutical industry's efforts to develop more effective drugs and vaccines. The size of the human genome is more than 180 times that of the peptic ulcer bacterium.

Developing in parallel with genomics is the area of gene expression, sometimes referred to as ''proteomics'' (Wilkins *et al.*, 1995). Its goal is to define the entire complement of proteins expressed by a genome, by a cell, or by a tissue type. Unlike the cell's genome, which is a definitive entity, this can vary according to prevailing conditions, and from one tissue to another in a single organism. Therefore, the pattern of proteins expressed at a given time or under a given set of conditions is a measure of the cell's or organism's physiology; in other words, it provides a snapshot of its behaviour. The estimated number of expressed proteins in brewing yeast is 6 000 proteins, while that in humans is believed to be between 60 000 and 80 000. In yeast, about half of the proteins have been characterised; in humans, the corresponding figure is no more than 5 per cent. Thus, the great challenge is first to make the inventory and then to define the structure and function of the different proteins. The biotechnology opportunities that will be provided by such analyses are enormous, and an early target is the definition of disease states and subsequent identification of targets for drug development. Both infectious diseases and genetic disorders are equally amenable to this type of analysis.

Such is the power of bioinformatics that biological research itself may be shifting from the traditional observation-experiment to so-called ''data-mining'', which uses advanced information technologies to formulate and test hypotheses by ''mining'' the databases containing gene and protein sequences. As a result, innovative experiments can be undertaken *in silico* rather than *in vivo* or *in vitro*, so that only essential experiments need be undertaken. Databases of the type required are growing at a spectacular rate, and bioinformatics has utilised the World Wide Web very effectively to put new data rapidly into the public domain. Various non-scientific issues with major implications for biotechnology are appearing as a result of this explosive development. Among those that require urgent attention are:

- How should databases be maintained and managed in order to meet the growing demands of users?
- How and/or should access to databases be controlled?
- How should research priorities be established?
- How should the databases be financed?
- What are the roles of the public and private sectors?
- What training is necessary to establish bioinformatics as an interdisciplinary profession?

RESEARCH AND DEVELOPMENT PRIORITIES

If biotechnology is to become an increasingly important source of clean industrial products and processes, R&D efforts will need to focus on a number of priority areas. Among those that deserve prompt and focused research in the near future are:

- innovative products derived from biological sources that contribute to sustainability;
- wider exploration of biological systems (enzymes, micro-organisms, cells, whole organisms);
- greater emphasis on the use of bioconsortia, including establishing them and developing production and degradation processes based on them;
- novel methodologies for developing biological processes (biomolecular design, genomics);
- innovative biocatalyst technology for use in areas where conventional biocatalysts have not yet been exploited (*e.g.* the petrochemical industries);
- biological recycling processes that convert unused resources to useful substances;
- emphasis on engineering, especially large-scale engineering, process intensification, measurement, monitoring and control systems;
- greater emphasis on biodiversity and widening the search for novel genes (bioprospecting), a process that will require, in parallel, the construction of infrastructures such as culture collections, comprehensive biological databases, and the development of bioinformatics;
- focus on development and application of recombinant technology.

Case Study 3.1

AUTHENTICITY OF RECOMBINANT PRODUCTS: THE POST-TRANSLATIONAL PROCESSING OF HUMAN INTERFERON-γ

Many proteins of human therapeutic interest undergo structural changes following translation of their messenger RNA; these modifications include glycosylation (the addition of sugars) and partial cleavage of the protein. When these proteins are produced by recombinant DNA technology, it is crucial that the recombinant protein resembles the authentic human version as closely as possible. Variations in the protein structure have profound implications for the pharmaceutical industry, where the presence and the structure of the sugar side chains, for example, can affect the rate of clearance from the human body, the desired biological activity, and the immunogenicity of the protein. The quality of recombinant proteins is influenced by many factors, among which are the type of host cell used for production (microbial, insect, mammalian) and the environmental conditions under which the cells are cultivated. One protein that has been studied in great detail in this context is recombinant human interferon-gamma (Hu-IFN-γ).

Hu-IFN-γ is a protein that activates macrophages during an immune response and also has potent antiviral activity. It is a protein of 143 amino acids in length and oligosaccharide side chains may be linked to it at asparagine residues in positions 25 and 97 on the molecule. When Hu-IFN-γ is produced as a recombinant product in mammalian cell cultures, primary or macro-heterogeneity occurs, depending on whether both, one, or neither of these two asparagine residues are glycosylated. Further heterogeneity of the recombinant product results from variations in the number and sequence of the sugars in the oligosaccharide side chains; this is referred to as micro-heterogeneity. Over 30 glycoforms (molecular variants caused by this macro- and micro-heterogeneity) have been detected in cultures of Chinese hamster ovary cells producing recombinant Hu-IFN-γ. Finally, a third element of heterogeneity results from so-called proteolysis from the C-terminal end of the protein so that up to ten amino acids may be removed leaving a truncated product. Thus, the recombinant product may be composed of an extremely complex mixture of Hu-IFN-γ molecules. These data have great significance for determining the optimal stage for harvesting animal cell cultures in order to produce the most authentic product. Highly sophisticated and sensitive techniques are now available for monitoring protein quality. The evaluation and control of protein quality during the production process, in order to make the most effective product, is now an important task for the bioprocess engineer.

Source: Hooker *et al.*, 1995; Goldman *et al.*, 1997.

Case Study 3.2

ENVIRONMENTALLY ENHANCED PAPER CHEMICALS

The manufacture of poly(aminoamide) resins that are used to give wet strength to paper and packaging board involves epichlorohydrin-based chemistry. The polymerisation generates the unwanted formation of haloalcohols, principally 1,3-dichloropropanol (DCP) and 3-chloropropanediol (CPD) which accumulate in the product stream. Various strategies have been considered for removing these haloalcohols, including process modification and physico-chemical treatments. However, development of a biotechnological unit stage that could be incorporated into the existing manufacturing process and have no adverse effects on the wet strength performance of the resins, has been achieved by harnessing the activities of a dehalogenating bioconsortium.

The selected bioconsortium was obtained by enrichment isolation and consisted of two bacteria, *Arthrobacter histidinolovorans* and *Agrobacterium tumefaciens.* Both could mineralise DCP and CPD, but they acted synergistically to remove these chemicals when operating in a continuous process. In order to support the growth of the consortium, the resin stream was supplemented with low concentrations of phosphate and urea. Under conditions of continuous processing, the ratio of *Arthrobacter* to *Agrobacterium* was 1:4, and this consortium remained stable for up to five months in laboratory-scale stirred tank reactors. If the ratio shifted to less than 50 per cent *Agrobacterium*, a breakthrough of DCP into the product stream occurred. Similarly, perturbations leading to the complete dominance of *Agrobacterium* led to CPD breakthrough. However, the dynamic nature of the system meant that the ratio returned to the optimal level for dehalogenation if the reactor was allowed to recover from the perturbation.

The laboratory-scale process was scaled and integrated into an existing wet-strength resin plant (3 m^3) in which the total haloalcohols were reduced from ca. 8 000 ppm to less than 6 ppm at a process retention time of 6.8 hours. It is important to note that the process was introduced into a chemical plant which had not previously handled biological systems; initial scepticism over the perceived fragility and unreliability of biotechnology was overcome, and this continuous, septic, mixed-culture bioprocess has proved to be extremely robust and responsive to fluctuating production requirements.

Source: Hardman *et al.*,1997.

Case Study 3.3

CHEMICAL *vs.* BIOTECHNOLOGICAL ROUTES TO 7-ACS

Chemical route	Biotechnological route
1) *Process*	
Produce zinc salt of cephalosporin C	Convert cephalosporin C to keto-adipinyl-7-ACS by the enzyme D-amino acid oxidase
Treat with trimethylchlorosilane to protect functional groups	Spontaneous conversion to glutaryl-7-ACS
React with phosphorus pentoxide to produce imide intermediate	Convert to 7-ACS by the enzyme glutaryl amidase
Hydrolyse imide to produce 7-ACS	
2) *Disadvantages and advantages*	
Use of environmentally unfriendly (chlorinated) hydrocarbons and hazardous P_2O_5, trimethylchlorosilane) reagents	Wastewater COD increased (0.1 to 1.7 tonne per tonne)
Use of heavy metal salts	Gas emission reduced (7.5 to 1.0 kg)
High-temperature processing, so energy-expensive	Liquid disposal by incineration reduced (29 to 0.3 tonne)
	Distillation residues reduced (2 to 0 tonne)
	Residual Zn recovery reduced (1.8 to 0 tonne)
3) *Summary*	
The biotechnology route reduces the percentage of process costs used for environmental protection from 21 per cent to 1 per cent	

Source: Wiesner, 1995.

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EVALUATING THE CLEANLINESS OF BIOTECHNOLOGICAL INDUSTRIAL PRODUCTS AND PROCESSES*

- **Of the various tools that exist for evaluating the cleanliness of industrial activities, Life Cycle Assessment (LCA) is the principal one for evaluating the complete environmental impact of products and processes.**
- **LCA takes into account the full life cycle of an industrial activity.**
- **LCA requires attention to four distinct elements: definition of scope and goals, inventory analysis, impact assessment (including weighting) and interpretation.**
- **There needs to be international harmonisation of methodologies, including the setting of system boundaries, for assessing cleanliness.**
- **LCA has been applied to verify the cleanliness of competing technologies; the few analyses that have been made on biotechnological processes have supported their cleanliness.**

INTRODUCTION

Products and processes can be hazardous, that is, they may be injurious to human health and/or the environment. All process steps, including extraction of materials, processing of materials, manufacturing of a product, use of a product, and waste management following the use of a product, must be taken into account in assessing the impact on the environment.

Several tools exist for evaluating the influence of technical products and processes on the environment (Table 4.1). If both the damage to the local environment and the total pollution load on the global environment are to be assessed, appropriate tools have to be applied.

Environmental Management Systems (EMS) focus on auditing management systems, and to some extent on the environmental performance of organisations and companies. There are two internationally accepted ways of proceeding. The Environmental Management Auditing System (EMAS) of the European Union (decree ETW No. 1836/93) is a site-specific approach to continuous improvement of both the environmental management system and the techniques used to protect the environment. ISO (International Organization for Standards) has issued a set of regulations (ISO 14001 and following) which are valid for auditing the environmental management of organisations and companies. ISO regulations are not limited to a site-specific view and address environmental engineering more indirectly. EMS are not used for detailed evaluation of environmental impacts, which is carried out by means of other tools.

Risk Assessment (RA) calculates the likelihood that environmental safety limits may be exceeded or that adverse effects may occur. It usually combines the degree of sensitivity of the environment with the intensity of the disturbance to which this environment is exposed. It is often used to assess the risk of adverse effects on human health and the environment which are associated with specific hazardous activities or substances, *e.g.* use of toxic chemicals. The predicted environmental concentration (PEC) of a substance is compared with the sensitivity of the ecosystem (no effect concentration, NEC) as a ratio

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Table 4.1. **Comparison of different tools for evaluating environmental impacts**

Tool	Object	Time perspective	Spatial perspective	Input/output focus	Methodological elements	Effects investigated	Data demands
Environmental Management Systems (EMS)	Environmental management of companies	Retrospective and prospective	Defined site/area	Input and output	Auditing of management system and environmental performance of a company	Improvement of environmental impacts	Environmental, social
Risk Assessment (RA)	Substance/ hazardous activity	Retrospective and prospective	Defined site/area/substance	Output	Dispersion, dose effect, likelihood of adverse effects	Toxic effects on human health and environment targets	Substance properties, environmental
Technology Assessment (TA)	Technologies	Prospective	Site-specific	Output	Likelihood of adverse effects on environment	All on local and ecological environment	Environmental, social, technical
Environmental Impact Assessment (EIA)	Project	Prospective	Defined site/area	Input and output	Dispersion, dose effect and others	All effects on local social and ecological environment	Environmental, economic
Material Flow Analysis (MEA)	Product/substance/ total mass	Retrospective and prospective (time: one year)	Defined region or world	Input and output	Allocation, mass-balance, dispersion	Not effect-oriented	Processes, substance properties, environmental mass
Life Cycle Assessment (LCA)	Product/service	Retrospective and prospective	Not site-specific, global	Input and output	Allocation, mass-balance, dispersion, dose effect	Overall potential environmental impacts of extraction and emissions	Process, environmental

Source: Partially adapted from Wrisberg, 1997*b*.

PEC:NEC. The PEC can be described as a single value, *e.g.* the average concentration of the hazardous substance, or as a variation in the concentration in space and over time. Knowledge of the time and place of the activity is as essential as information about the probable intensity of the disturbance and the characteristics of the polluted environment. Risk Assessment does not assess global environmental problems, such as the greenhouse effect, and it does not cover the entire life cycle of a product or service.

As a prospective instrument, *Technology Assessment* (TA) reveals the likelihood of social, economic and environmental effects associated with technologies, *e.g.* nuclear power generation. TA is an attempt to establish an early warning system to detect, control and direct technological changes and developments in order to maximise the public good while minimising the public risks. It regards technical development as a social process that should be guided by political decisions to maximise public welfare. As the first step, the goal and the system have to be defined. Following a detailed analysis and structuring of possibly affected areas, the nature and degree of potential impacts are determined and assessed. As a final step, alternative options are discussed. TA is a tool to support the decision-making process at a political level.

Environmental Impact Assessment (EIA) identifies and evaluates local impacts on the physical and social environment of a specific project or activity, *e.g.* the building of a new production plant. It is used for a prospective assessment of environmental impacts at a very detailed, site-specific level. All components of the local environment – air, water, soil, ecosystems and reciprocal effects – are evaluated. Several steps similar to a Technology Assessment have to be performed. In a screening, it is stated whether an EIA is needed. The goal and depth of the assessment are provided in a definition of the scope. The expected environmental impacts are recorded and assessed. The final step is to decide whether a permit is to be given for a planned project and determine the measures for minimising environmental impacts. As a project-oriented tool, the EIA does not include all the steps of the life cycle of a product or service.

A Mass Flow Analysis (MFA) quantifies the pathways of mass out of and through the environment over a certain period in a specific economic region. It also reveals the sources of resource consumption and pollution and the sinks in a defined region. An MFA simply gives an inventory of inputs and outputs without predicting potential or even actual environmental impacts connected with the flows. In the first step, the system is defined and described by products, processes, or by one or more substances. After measuring product flows and the substances contained, mass flows are computed. The laws of conservation of energy and matter are valid. The final step provides a systematic graphic representation and an interpretation of the results. Relevant processes which indicate the successful management of mass flows are identified.

Life Cycle Assessment (LCA) evaluates potential environmental impacts of products or services with reference to their entire life cycle (“from the cradle to the grave”). LCA takes a global approach. It is not concerned with the place and time at which a product is made, used or disposed of. Emissions and extraction of relevant substances are recorded and assessed on the basis of the total involved. LCA reflects the load of environmental stresses, but not the concentrations emitted or their variations. It is often used to reveal the most hazardous steps in the life cycle of a product and to decide which of several product alternatives is associated with the least potential impact on the environment. Potential effects are recorded, as it is not possible to obtain the data required for predicting actual effects on the environment. Potential effects can serve as indicators for actual effects. LCA is part of “responsible care” (see Box 4.1).

LCA is currently the method of choice for assessing the cleanliness of industrial processes. It is the best method for determining the increased degree of cleanliness that may be achieved by introducing biotechnological processes.

If industrial products and processes are to be subjected to a critical appraisal from the viewpoint of sustainability, the attractiveness of LCA lies in its:

- use of the life cycle concept for products/systems;
- description of impacts on the ecological system;

Box 4.1. **Responsible care**

Responsible care was first defined by the chemical industry and represents the chemical industry's world-wide commitment to continual improvement in all aspects of health, safety and environmental performance and to openness in communicating its activities and achievements. Today, most other industries also develop responsible care programmes.

National chemical industry associations are responsible for the detailed implementation of responsible care in their countries and each responsible care programme incorporates the following fundamental features:

- a formal commitment on behalf of each company to a set of guiding principles, signed in most cases by the chief executive officer;
- a series of codes, guidelines and checklists to assist companies in implementing the commitment;
- the progressive development of indicators against which improvements in performance can be measured;
- an ongoing process of communication on health, safety and environmental matters with interested parties outside industry;
- provision of platforms for companies to share views and exchange experience on implementation of their commitment;
- adoption of a title and a logo which clearly identify national programmes as consistent with and part of the concept of responsible care;
- consideration of how best to encourage all member companies to commit themselves to and participate in responsible care.

The responsible care programmes of individual countries are at different stages of development and have different biases.

Responsible care can include:

- product responsibility;
- dialogue;
- environmental protection;
- safety in the workplace;
- plant safety and hazard management;
- transportation safety.

- opportunity for ecological optimisation, including feedback between parts of the life cycle chain;
- possibility of objective or fair comparisons of ecological systems;
- easier objective communication of ecological problems.

LCA studies also have limitations, which should not be disregarded. They cannot:

- determine the overall impact of a product or a group of products on the environment;
- evaluate parameters, such as availability and renewability of raw materials;
- compare products produced for different purposes and/or under different conditions;
- provide generalisations on methods of disposal;
- determine decisions (although they can support decision makers).

Although LCA was developed a quarter of a century ago, it has so far had little impact in the bioprocess and bioproduct sectors. Only recently have concerted efforts been made to harmonise the methodologies involved to give greater credibility to and confidence in LCA. The use of LCA, particularly by small companies, may be hindered by cost and time constraints and by the amount of resources required to analyse complex products. Inventory calculations are made difficult because the energy and raw materials inputs and waste outputs are usually not controlled by a single company and it may be impossible to obtain the relevant data.

The environmental impact of a product or process is of primary concern. To assess this, it is necessary to identify what information is required, how it can be collected, and how reliable it is. Goals that need to be borne in mind are the preservation or efficient use of natural resources and the reduction or optimisation of pollution by emissions and waste. These goals concern the environment as a *source* and a *sink*, and they comprise both the minimisation of pollution and its optimisation in cases where the minimisation of one parameter is coupled with the increase of another. It is precisely with regard to such considerations that the importance of LCA studies emerges.

LIFE CYCLE ASSESSMENT

The purpose of LCA is to support industry and government decision-making processes for the setting of priorities, strategic planning, product and process development. LCA is confined solely to describing ecological aspects of an activity. Socio-political and economic decisions do not fall within the scope of LCA, although both have an equal claim to relevance when it comes to decision-making processes by government and industry. LCAs should be presented in such a way that they enable decision makers to weigh the various ecological, economic and social aspects, and findings should be tailored to the individual needs of the decision maker. However, if, for technical or economic reasons, one of several competing products has overwhelming advantages, LCA will normally not be necessary.

LCA consists of four steps: definition of aim and scope (including definition of system boundaries), inventory analysis, impact assessment (including weighting), and interpretation (for a detailed presentation of LCA methodology, see Annex 4.1). Because it investigates the environmental aspects of a product's entire life cycle, LCA needs to determine and evaluate potential effects on human health, the environment, and the use of natural resources, from raw material acquisition through production, to subsequent use and disposal. There is a high degree of consensus on the methodological framework, which has been incorporated into the ISO draft standards (see Annex 4.2).

If LCA is to become the primary analytical tool for measuring the cleanliness of industrial operations, it must secure legitimacy (credibility of methods and conclusions) and strive for international harmonisation. The very different energy policies of the member states of the European Union, for example, illustrate the difficulty. In this respect, the on-going work of SETAC and ISO is very important. ISO's Technical Committee 207, charged with developing standards in environmental management, has a subcommittee (SC5) devoted to LCA (ISO 14040, 1997).

Aim and scope: defining the boundaries and inventory analysis

For an LCA, the first task is to define aim and scope and to tailor the assessment to its intended application. More exacting demands can be made of LCA studies to be used for political decision-making processes, which are likely to have far-reaching consequences for the economic sectors concerned, than for in-house analyses of shortcomings.

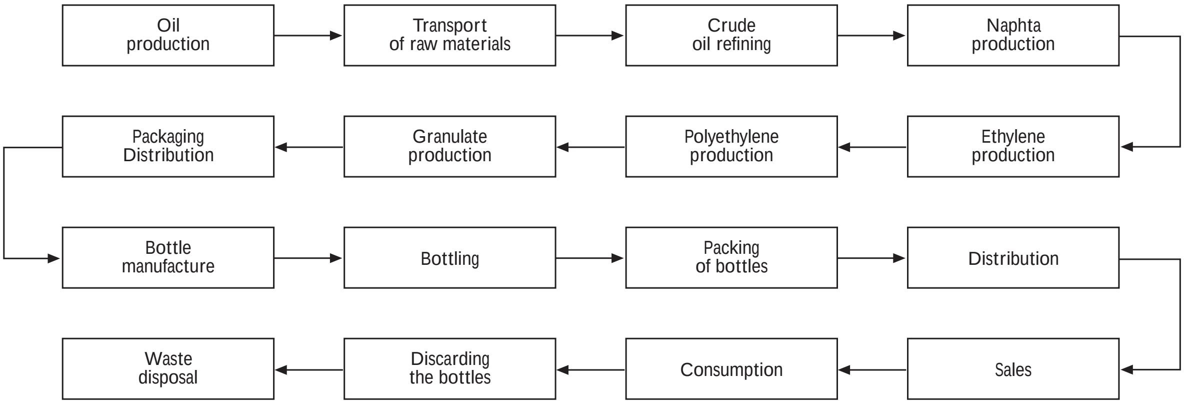
System boundaries are the interface between the product system under consideration and the environment or other product systems (ISO 14041, 1997). They depend on many factors, such as the application, target group, assumptions made, cut-off criteria, data and cost constraints. As these boundaries can significantly influence the result of an LCA, the criteria used to determine them need to be described in detail.

To compare product systems, the comparability of the systems investigated must first be ascertained. This means applying the same scope and parameters (functional unit, system boundaries, data quality, allocation procedures, criteria for assessing input and output flows, and criteria for impact assessment).

An inventory is made by collecting data from the relevant inputs and outputs (*e.g.* use of energy and resources, emissions into the environmental media (water, soil, air). Great caution should be used when making comparative assertions without prior impact assessment, as inventory results rarely prove the absolute superiority of a system.

An exhaustive analysis of a product's life cycle has to take into consideration not only the mass and energy flows linked to raw materials acquisition and production processes, but also those related to transportation, use and disposal. Figure 4.1 shows, for example, the many elements in the life cycle of a relatively simple product such as a polyethylene bottle.

◆ Figure 4.1. ***The life cycle of a polyethylene bottle***



Source: SETAC, 1993*a*.

Pollution caused by various product systems cannot necessarily be clearly differentiated, so that it is difficult to ascribe different types of pollution to the various systems. Similarly, material flows from a process under consideration may not leave the system as waste but may be used in a second process not under consideration.

In practice, there are often limitations on the labour-intensive task of data acquisition. In the course of an LCA, unavailable data and/or limited access to data and lack of time and capacity can mean that not all inputs and outputs will be measured. Therefore, decisions have to be made concerning which processes should be investigated and in what detail.

Impact assessment

In terms of the four steps of an LCA, the definition of goal and scope is the least difficult, and a consensus on procedure is gradually taking shape for inventory despite a few unresolved questions relating to methods and practical matters.

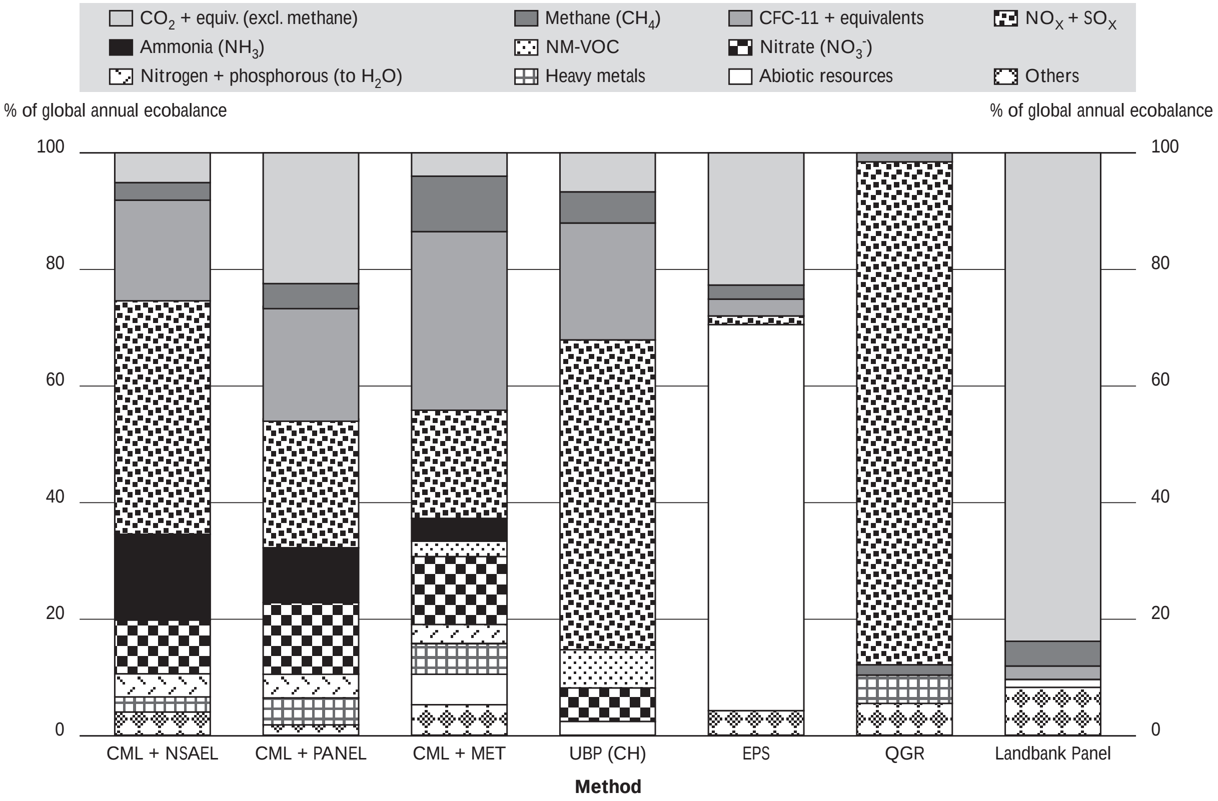
The same cannot be said of impact assessment (ISO 14042, 1997). Over the past few years, many methods of assessing impacts have been developed The function of impact assessment is to examine the data (mass and energy flows, environmental releases, etc.) and to assess all these elements for their possible environmental consequences. It is widely accepted that the areas to be protected are human health, the natural environment, and resources. Where possible, life cycle impact assessment aims to take a quantitative approach. However, in some cases, value-based judgements may be used to define categories and develop category models.

Weighting is the assignment of relative importance to the factors included in a LCA. This is a key element in LCA and results in a comparison of systems across categories. Weighting is the most strongly disputed aspect of LCA, as it is not based on scientifically verified and/or generally recognised rules. It is strongly connected with values and therefore has subjective aspects. Various procedures have been developed, each with its own specific advantages and disadvantages. The assessment process that accompanies the weighting can be described as "the interlinking of available information pertaining to a set of given facts with a personal value system to form a judgement about the facts themselves" (Giegrich *et al.*, 1995). It would, therefore, be misleading to speak of an "objective weighting". This does not mean, however, that weighting is necessarily arbitrary. It is crucial that all the issues involved should be presented so clearly and precisely that outsiders cannot fail to understand them.

The weighting of the individual factors and of their environmental impact is the single largest difficulty in establishing an LCA. While some people argue for establishing the magnitude of impacts by taking individual quantitative factors, adding them together, and drawing conclusions or making decisions on the basis of the total, others argue that an LCA can only summarise the factors involved but that the actual interpretation or weighting of different emissions (*e.g.* CO_2 *vs.* mercury in the soil) and the conclusions drawn from that interpretation remain part of the responsibility of the political or economic decision makers.

Figure 4.2 illustrates the different assessment methods made possible by using global emissions and environmental interferences for comparison purposes. The estimated total annual global amount of all emissions is considered to be the total "ecobalance". The comparison shows a wide range of

◆ Figure 4.2. ***Findings of a global LCA using different impact assessment methods***



CML + NSAEL:	Characterisation methods according to Centre for Milieukunde Leiden (CML), combined with a "distance to target" approach, based on "no significant adverse effect level" (NSAEL).
CML + PANEL:	CML characterisation combined with a Dutch panel.
CML + MET:	CML characterisation combined with an ecological scarcity approach, based on the Dutch national environment plan.
UBP (CH):	Ecological scarcity approach combined with Swiss pollution aspects.
EPS:	Environmental Priority Strategies (EPS), calculated using the standard values derived from a public opinion poll.
QGR:	Quality Goal Relation (QGR), with consideration given to environmental media.
Landbank Panel:	Panel assessment, based on a multi-stage poll of environmental experts.

Source: Förster, 1994.

priorities; this is partly due to the different methodologies and partly to the use of different sets of data for weighting. The different methods do not all seek the same goals, and this automatically results in differences in impact assessment. However, it can be shown that most impact assessment methods can describe over 90 per cent of global impacts using a relatively low number of emissions or resources. High priority is often given to global warming and ozone depletion and low priority is generally given to use of land. The Landbank Panel places extremely strong emphasis on global warming (over 80 per cent) and the Environmental Priority Strategies (EPS) method on use of resources (approximately 70 per cent). Such a clear setting of priorities should be subjected to close scrutiny. There is a general consensus that the following impact categories require consideration: depletion of resources, global warming, and ozone depletion. Further categories are the subject of ongoing discussion.

It can be stated categorically that the goal of an LCA is not to determine the impacts *actually* caused by a product according to these categories, because in many sectors the scientific underpinnings and corresponding data are simply not available. The assessment refers to *potential* environmental impacts from the key elements in the inventory.

The following list of 15 impact categories are the object of international agreements for the protection of the environment, such as the Rio Declaration, Agenda 21, or the Montreal Agreement (Heijungs, 1992):

– depletion of abiotic resources;
– depletion of biotic resources;
– global warming impact;
– ozone depletion;
– human toxicity;
– aquatic ecotoxicity;
– terrestrial ecotoxicity;
– formation of photochemical oxidants (“summer smog”);
– acidification;
– nutrification;
– waste heat via wastewater;
– odour pollution;
– noise;
– damage to ecosystems and landscape;
– victims (human).

There are somewhat simplified LCA studies based on energy and mass alone, which can nonetheless provide important information and indicate cases of severe pollution. Strictly speaking, energy consumption does not constitute an environmental impact, although it is recognised as a crucial problem area. Environmental pollution linked to energy provision and distribution has a tremendous influence on the animate and inanimate environment.

LCA IN PRACTICE

The history of Life Cycle Assessment goes back more than 20 years (Rubik and Teichert, 1997). A start was made in 1974 with a study carried out by Batelle, a German consultancy (Oberbacher *et al.*, 1974). More than 600 assessments in Germany, Italy, Sweden and Switzerland have been reviewed (see Annex 4.3).

Almost no LCA studies were carried out before the beginning of the 1980s, but their numbers increased from the mid-1980s and gained momentum in the 1990s. In Germany, there have been at least 16 studies a year since 1990; in Switzerland the number of LCA studies has stood at 15-20 a year during the present decade; and in Sweden the upsurge began in about 1992, and since then, almost the same number of studies has been recorded as for Germany.

In Germany, companies commission most LCAs, followed by government (at a much lower level) and trade associations. In Switzerland, academia follows closely behind industry, and in Sweden and Italy the private sector predominates. However, the role of the public sector should not be underestimated, as LCA studies commissioned by the public sector have repercussions in the private sector. Some instruments of national, product-oriented environmental policy (Oosterhuis *et al.*, 1996; Rubik and Teichert, 1997) refer explicitly or implicitly to LCA or life cycle thinking, as in the case of the German "blue angel" eco-label scheme and the new German waste management act (*Kreislaufwirtschafts- und Abfallgesetz*). The European eco-label scheme is explicitly based on the results of LCA studies.

In addition to public policy, the market can strongly motivate businesses to adopt LCA. As retailers and consumers demand information on the environmental characteristics of products, some companies use the results of their LCA studies for their marketing strategies and competitors are sometimes forced to react by presenting their own LCA-based information. In Germany, reaction to consumers' increased environmental awareness outranked all other influences. Retailers and consumers are such a powerful market force that their purchasing attitudes can influence producers' attitudes and push them towards an environmentally oriented course (see also Chapter 5). Public policy and the market have also stimulated enterprises or a sector to carry out joint LCA studies. Examples can be found in the automobile and chemical industries.

Environmental protection appears chiefly to be a concern of management, since within companies, the impetus to conduct LCA studies has come largely from management. The cost-reducing potential, notably in terms of lower use of resources, is also not without significance, and many businesses have realised that environmental protection and profitability are not necessarily mutually exclusive.

In Germany, the chemical and the automotive industries are the largest commissioners of LCAs. The food processing and luxury foodstuffs industries are also significant. An analysis of companies by size shows that large-scale enterprises compile or commission most LCAs. In Switzerland, the rubber and plastics processing industry is the most important commissioner of LCAs, followed by the handling and processing of non-metallic minerals/glass manufacture and processing. In Sweden, the drive comes from electrical engineering, while in Italy, the chemicals industry and electrical engineering have the largest share. A comparison of product groups shows a broader industry distribution; nevertheless, three industries, automotive, construction and packaging, predominate.

The level of in-house competence and experts is often important. For instance, the multinational Procter & Gamble employs a staff of 15 world-wide, whose work solely concerns LCA. Dow Chemical and Volvo each employ six persons in this area (Atlantic Consulting *et al.*, 1996).

Biotechnologies and biotechnological products

According to available studies, biotechnology appears to be underrepresented in LCA studies. Examples are found in the areas of cleansers and detergents, where LCA has been used for individual substances (enzymes and tensides), in waste technologies, and in the renewable raw materials sectors.

While methods of measuring the cleanliness of industrial products and processes are available, their application is still in the development phase. There are many industry publications on the treatment of solid waste, wastewater, and emissions, but they are infrequently linked to the products manufactured and only in exceptional cases to the resources used.

Reliable published data are even rarer for biotechnological processes or products than for chemical processes. A comparison of chemical and biotechnological processes in the form of a sound LCA is the exception rather than the rule.

DETAILED EXAMPLES

To date, well-defined, generally accepted LCAs have only been carried out for individual cases. It should be recalled that, like all the information contained in this chapter, only publicly disclosed studies are discussed. It is generally assumed that there are many in-house LCA studies about which no information is available.

Example 1. Enzymatic *vs.* chemical clean-up processes

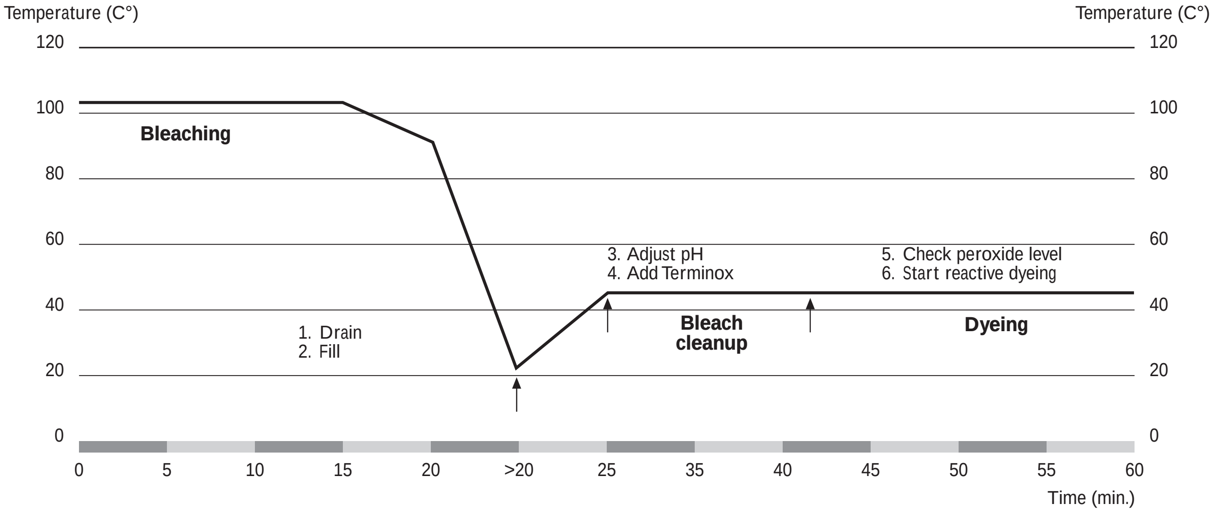
Novo Nordisk A/S, Denmark, has published data on their process for removing residual hydrogen peroxide after bleaching prior to dyeing. This step in the process of textile production is called bleach clean-up. This step uses the enzyme catalase (Terminox Ultra®) which has the following advantages: it has no adverse effects on dyestuffs, there is no need to heat or rinse prior to dyeing, no risk of harmful overdosing, no formation of by-products in wastewater. Catalase is biodegradable and is not toxic for aquatic organisms.

Novo Nordisk has published the data from a comparison between three different methods of bleach clean-up:

- Cold rinses: bleaching → overflow rinse → rinse → rinse → rinse → dyeing.
- Use of reducing agents: bleaching → overflow rinse → reducing agent → rinse → dyeing.
- Catalase (Terminox Ultra®): bleaching → overflow rinse → Terminox Ultra® → dyeing.

The process step for using catalase is outlined in Figure 4.3. The enzymatic treatment period is about 20 minutes, the temperature for bleach clean-up and dyeing is the same.

◆ Figure 4.3. ***Bleach cleanup with Terminox Ultra*®**



Source: Novo Nordisk, 1997.

Production of the enzyme has to be taken into account when an LCA is made for the whole process. Novo has calculated the life cycle inventory for 10 l of a catalase-liquid batch (see Table 4.2). A comparison of the amount of water used in the bleach clean-up process shows that by using the enzyme, the dye-house saves 6 300-19 000 l water per tonne of textiles. By substituting the enzyme for a reducing agent in a hot rinse, additional savings of 1.6-1.8 GJ/tonne of textiles can be made, and, owing to the reduced energy consumption, release of CO_2 is lowered by 100-120 kg/tonne of textiles produced.

Table 4.2. **Life cycle inventory for 10 l Terminox Ultra®**

Use of resources		Wastewater emissions	
Water	7 m^3	Suspended solids	0.3 kg
Land	0.03 ha × yr	BOD	0.2 kg
Coal, oil, gas/non-fuel	260 kg	COD	0.5 kg
Minerals	320 kg	Total N	0.21 kg
		Total P	0.38 kg
Use of energy		Sulphate ions	28 kg
Total energy consumption	14 GJ	Chloride ions	1.7 kg
		Fluoride ions	0.8 kg
Emissions into the air		Metal ions	0.061 kg
Carbon dioxide	1 400 kg	Acid as H^+	0.028 kg
Sulphur oxides	7.5 kg	Hydrocarbons	0.018 kg
Nitrogen oxides	5.5 kg	Oil	0.016 kg
Particulates	1.1 kg	Phenols	0.0002 kg
Hydrocarbons	6.6 kg	Pesticides	0.001 kg
Other organics	0.012 kg		
Metals	0.0003 k	**Solid waste**	
Hydrogen sulphide	0.0014 kg	Industrial waste	50 kg
Hydrogen chloride	0.006 kg	Mineral waste	7 kg
Hydrogen fluoride	0.0003 kg	Slag and ash	20 kg
		Non-toxic chemicals	20 kg
		Toxic chemicals	0.0025 kg

Source: Novo Nordisk, 1997.

Example 2. Stonewashing of jeans

Jeans are one of the world's most popular clothing items (Kothuis and Schelleman, 1996; Umweltbundesamt, 1995). During the production process, indigo is used to colour the fabric. The "stonewashed look" is one of the many available appearances of jeans. This is achieved by locally removing the indigo colour using a process in which pumice stone is added to the washing drum to abrade the garment. Enzymes can be used to facilitate the abrasion of the indigo dye from the yarn surface. In practice, three washing methods are used:

- stone washing with pumice only;
- stonefree washing with enzymes only ("biostoning");
- washing with a combination of pumice and enzymes.

Today, biostoning is the main stonewashing process used in the jeans finishing industry. This shift occurred during the past decade, owing to the following factors:

- process economics: biostoning has lower processing costs;
- look: the look of pumice-washed jeans is different from that of biostone-washed jeans and each meets a specific market demand;
- environmental impact: although biostoning has environmental advantages, this did not play an important part in company decision making.

LCA comparing biotechnological and chemical technologies

LCA was performed on these three methods for reducing the indigo content on the outer layer of the jeans, using neutral cellulase and pumice stone from Turkey. Of the various process steps used in a jeans finishing centre, three specifically relate to the production of stonewashed jeans, namely: stone washing, wash off (removal of the stones), and wash (clean-up of the garment). Only these three steps were covered by the LCA concerned.

The product under examination was a type 501 jeans from Levi Strauss & Co., finished in Antwerp, Belgium. The jeans are "stonewashed" at the end of the production process. The system boundaries for the LCA included the mining of the pumice, the production of the cellulases, transport, and finally the jeans finishing process. The main inputs and outputs for the LCA were defined as the energy, raw materials, aiding compounds, and releases that contribute to the product's environmental impact. The data inventory was classified, a process in which the amounts of substances are converted into a score for their contribution to a number of environmental themes. The environmental scores can then be added to estimate the product's total contribution to specific environmental themes.

LCA results

The LCA results show that the biostoning method scores best in almost all respects. The "combined" washing method scores best for "human toxicity: water", because of relatively higher emissions of phosphorus compounds into water from the biostoning method. The pumice process scores best for "odour" mainly because of the ammonia emissions from agriculture and from the production of ammonia for fertilisers used in production of the raw material for cellulase fermentation. Table 4.3 summarises the LCA results.

Table 4.3. **LCA results for the "stonewashing" process**

Environmental effect	Pumice	Pumice + cellulase	Cellulase
Energy value of fuels (GJ)	1.0	0.7	0.6
Chemical oxygen demand	5.2	3.8	3.1
Human toxicity: air	0.7	0.3	0.1
Acidification	0.6	0.2	0.1
Nutrification	0.2	0.2	0.1
Photochemical effect	0.1	0.1	0.1
Odour	1.9×10^{-4}	4.9×10^{-4}	7.9×10^{-4}
Human toxicity: water	2.0×10^{-3}	4.6×10^{-5}	7.4×10^{-4}
Ecotoxicity, aquatic	4.6×10^{-2}	1.6×10^{-2}	1.2×10^{-3}
Global warming effect	62.6	44.5	35.7

LCA classification results for the three different stonewashing methods

With regard to air, water and waste, an economic cost comparison based on environmental regulations or needs was made for the three stonewashing methods. The highest costs are for removing the pumice from the wastewater, the emissions of chloride ions and chemical oxygen demand (COD) from the water and CO_2 and hydrocarbons from the air. These costs will increase if potential future standards for sustainable development are to be met.

The highest economic costs based on environmental regulations or needs arise from wastewater treatment (Table 4.4). With all stonewashing methods, the costs for water emissions are about 75 per cent of all environmental costs.

Table 4.4. **Comparison of total economic costs**

$/100 kg jeans

Environmental economic costs	Pumice stonewashing	Pumice + cellulase	Cellulase
Air	8.31	5.57	4.13
Water	28.10	20.16	16.37
Waste	2.01	1.26	0.62
Total	38.42	26.99	21.12

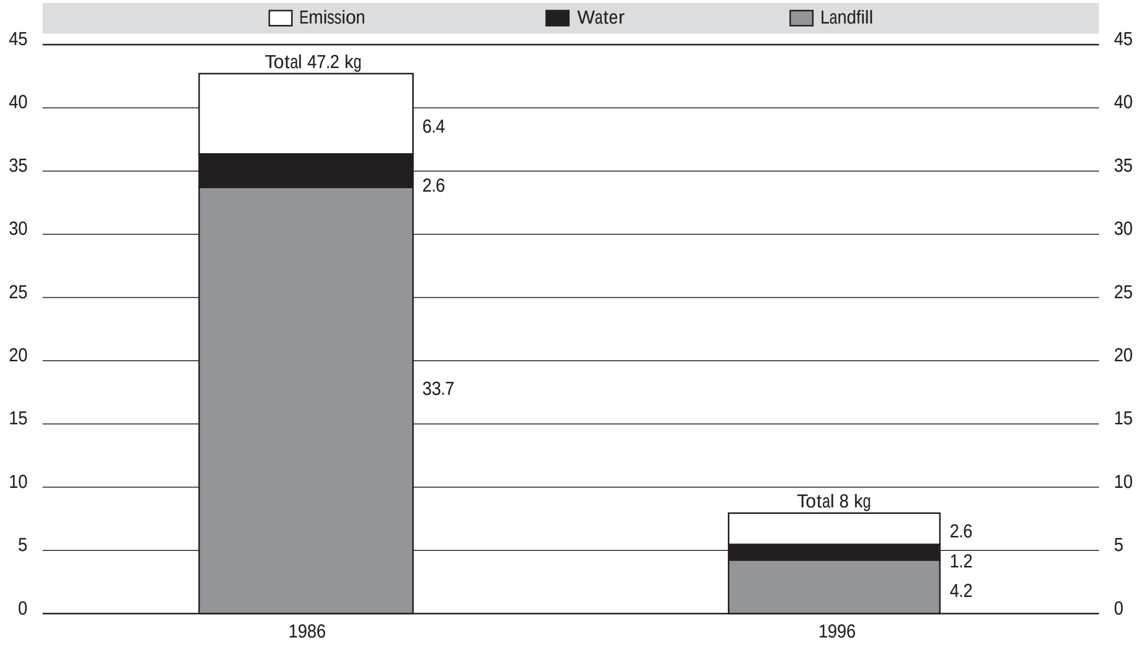
Conclusions

On the basis of the LCA, it seems justified to consider the biostoning process as more environmentally friendly than the pumice stoning process. However, this was not the driving force behind the industrial success of this process; instead, the traditional process was replaced for reasons of economics and quality.

Example 3. Reduction of production-related waste

To give an idea of the development of environmental protection in production, BASF published comparative figures for a number of years in its *Environmental Report 1996* (Figure 4.4). Pollution per tonne of products was 42.7 kg in 1986, but only 8.0 kg in 1996. In 1996, the manufacture of 8.1 million tonnes of products produced an average of 0.8 per cent of material which entered the wastewater, waste air, or was disposed of. This perceptible drop in production-specific pollution can mainly be traced to the use of remediation technology, such as waste gas and wastewater purification plant, residue incineration, and controlled landfilling. The consistent application of the concept of "avoid, reduce, reuse" from the planning stage of processes and plant onwards means a further reduction in the occurrence or development of waste or emissions.

◆ Figure 4.4. ***Reduction of production-related waste***



Example 4. Eco-productivity index

Novo Nordisk in Denmark minimised the impact of their operations on the environment by developing more environmentally sound processes and by reducing emissions, consumption of raw materials, and energy. All relevant data were published by Novo Nordisk in 1995.

To illustrate the effect, an eco-productivity index (EPI), an indicator of resource utilisation, is calculated. An EPI indicates the effectiveness of the use of resources in production in the course of one year. It relates the scale of the production to the consumption of raw materials, water or energy. The EPI is calculated as follows:

EPI = Indexed turnover in constant prices × 100/indexed resource consumption. Where 1990 = 100.

The turnover index (volume/product mix) is adjusted to accommodate fluctuations in exchange rates and prices. Table 4.5 gives an example of an EPI for raw materials from 1990 to 1995.

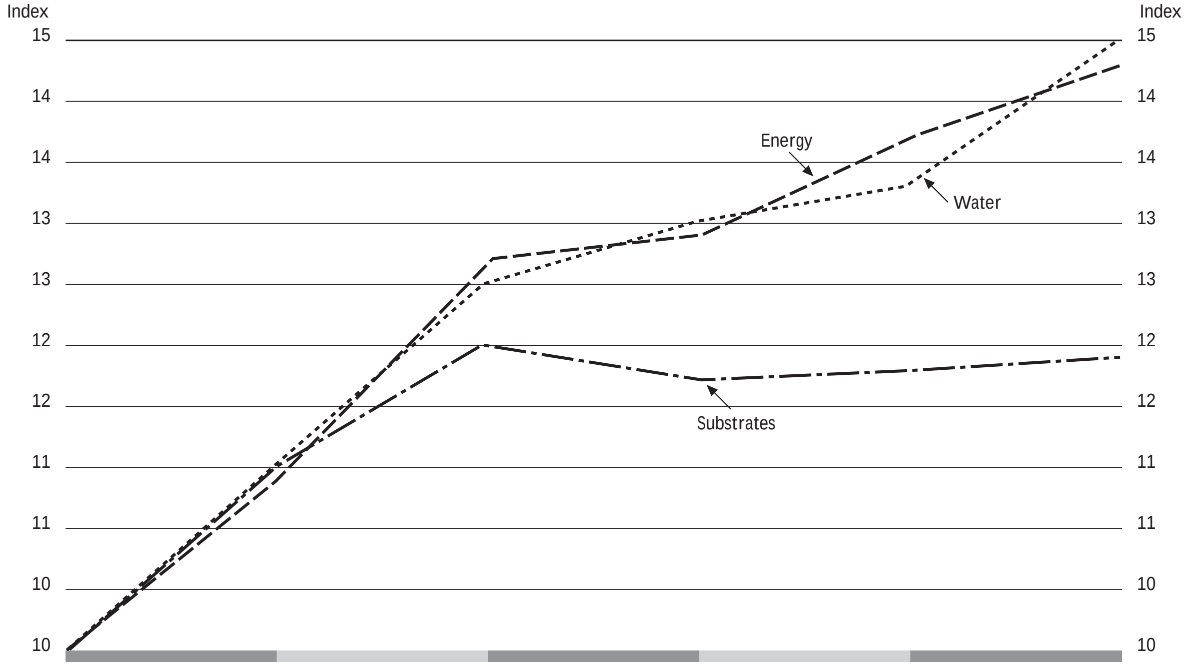
Table 4.5. **Example of an EPI for raw materials**

	1990	1991	1992	1993	1994	1995
Enzyme production: adjusted turnover = volume/product mix	–	22%	21%	22%	14%	8%
Adjusted turnover index	100	122	148	165	188	203
Quantity of raw materials in 1 000 metric tonnes	159	169	187	214	244	261
Index of raw materials	100	106	118	135	153	164
Eco-productivity index B × 100/D	100	115	125	122	123	124

The higher the EPI, the better the use of a specific resource. Figure 4.5 shows the trend in EPIs from 1990 to 1995. Water consumption increased from 3.75 to 4.78 million cubic metres and energy consumption from 3.02 to 3.88 GJ. Novo Nordisk has set the following 1995-97 targets for consumption of raw materials (substrates), water and energy for production and products:

- average annual increase in raw materials eco-productivity of 2 percentage points;
- average annual increase in water eco-productivity of 5 percentage points;
- average annual increase in energy eco-productivity of 4 percentage points.

◆ Figure 4.5. ***Eco-productivity index***



Source: Novo Nordisk, 1995.

Example 5. rDNA technology for reducing environmental pollution

COGNIS GmbH (Henkel) in Germany has published an LCA of detergent proteases in which the fermentation of recombinant and unmodified micro-organisms is compared (Bahn and Intemann, 1997) (for further details, see Case Study 4.1, page 106).

Detergent proteases, which remove protein impurities, are essential components of modern detergents. Because of their catalytic effect, low concentrations (0.1-1.0 per cent) of proteases are used. Similar washing performance cannot be achieved by substituting other substances or by raising the washing temperature.

The LCA compares the production processes for proteases based on an organism optimised by classical selection processes and on a recombinant organism. The immediate objective of the LCA was to determine the pollution linked to enzyme production and to reveal any weaknesses in the enzyme production. A further objective was to assess the ecological potential of genetic engineering methods.

The assessment covers not the whole life cycle of detergent proteases but only enzyme production, including all processes from production of raw materials to the finished granulate. Consideration was also given to the transport of the raw materials used during enzyme production from the individual manufacturers to the enzyme producers. No attention was given to buildings, apparatus, etc., as enzyme production is an energy-intensive and mass-intensive process in which the infrastructure plays only a very minor part.

Protease production yields only one useful by-product, an organic fertiliser that is produced from the biomass resulting from protease production. The sludge is first mechanically drained and then dried thermally to achieve a highly nutritive fertiliser.

Inventory

To produce 1 kg of enzyme from the conventional organism requires a total of 3.54 kg raw materials, but to obtain a quantity with an equivalent washing performance from the recombinant organism requires only 2.34 kg, a reduction in raw material demand of 34 per cent.

The change from conventional production to production by means of genetic engineering reduces the demand for process energy by 60 per cent from 131 MJ/WP to 52 MJ/WP (megajoules/washing performance). The production of the Henkel Group's annual requirements results in primary energy savings of approximately 420 000 GJ. This corresponds to the annual primary energy consumption required for the laundry purposes of about 170 000 households or 380 000 persons.

Besides the input factors, emissions also have to be calculated. Table 4.6 summarises the aggregate emissions of the various detergent proteases over the total production chains.

Given the company's annual demand, application of the new enzyme produced with recombinant organisms made it possible to reduce the annual emissions by approximately 30 000 tonnes of CO_2, 170 tonnes of carbon and 190 tonnes of sulphur dioxide.

Impact assessment

If the findings of an LCA are to be collated, the individual sources of pollution have to be compared and weighted. As noted above, weighting depends to a considerable extent on priorities. For instance, in the 1970s, energy consumption played a vital part in the assessment of environmental impacts. In the 1980s, the pollutants responsible for the death of forests superseded energy demand as the most important criterion. In the 1990s, CO_2 emissions and the ensuing global warming have become the number one topic.

Within the framework of this LCA, atmospheric emissions were assessed in terms of impact on global warming, development of acid rain, and smog formation. Aquatic emissions were assessed according to the yield of nutrients in waters and related oxygen consumption. The impact assessments clearly confirm the general claim that the use of a genetically modified strain can reduce the consumption of energy and resources and the pollution in the form of emissions by a factor of 3-4.

Table 4.6. **Emissions for the total enzyme production chains of detergent proteases**

	Unit	Conventional organism	Recombinant organism
Atmospheric pollution			
Total carbon dioxide	g/WP*	8 507	3 422
– From renewable raw materials	g/WP*	1 548	849
– From fossil raw materials	g/WP*	6 959	2 572
Hydrocarbons	g/WP*	67	36
Sulphurous oxides	g/WP*	60	25
Nitrous oxides	g/WP*	49	15
Dusts	g/WP*	24	7
Carbon monoxide	g/WP*	14	2
Wastewater pollution			
Chemical oxygen demand	g/WP*	158	77
Biological oxygen demand	g/WP*	7	4
Waste			
Organic waste	g/WP*	1 033	313
Slag/ashes	g/WP*	98	26

WP* = Amount of enzyme whose washing performance corresponds to 1 kg conventional enzyme.

Example 6. Bioethanol production

Ethanol can be produced both biotechnologically and synthetically. In 1991, world-wide annual production of ethanol was 15.1 million tonnes, of which 12.6 million produced from agricultural resources and 2.5 million from fossil fuel feedstocks. In terms of volume (excluding beverage production), ethanol is the most important biotechnological product. In financial terms, it is only exceeded by antibiotics production.

Case Study 4.2 (page 110) compares the production of bioethanol with synthetically produced ethanol. The goal of the study was to establish the feasibility, in principle, of an LCA for products of biotechnological processes, along with a description of the system and the boundary conditions as well as an interpretation of the findings.

Bioethanol is made from sugar, which may be derived from crops such as sugar cane, beet, or maize. When it is made from sugar cane, the cane is crushed and the sugar is extracted using water. The residue, known as bagasse, may be used to generate steam for the subsequent processes. Yeast is used to ferment the sugar, and the ethanol is removed by distillation. Burning the bagasse for fuel means that the part of the ethanol production process, from the cane crushing stage to obtaining 94.5 per cent ethanol by distillation, is self-sufficient in energy. The waste from the distillation process is known as stillage and may be discarded or used for fertiliser or animal feeds. Overall, producing 1 kg of ethanol requires 16.8 kg of cane and yields 14.8 kg of stillage.

Because the information available on water and soil pollution was inadequate, the study did not address these environmental parameters.

Data for ethanol produced from grain and sugar cane were compared with the values documented in other studies, *e.g.* Parisi (1983), which gives a comprehensive survey of studies on ethanol production from sugar cane, sugar beet, grain and other raw materials. They agree within a certain scatter. Results for the production of ethanol from sugar beet, which is also copiously documented, are of the same order of magnitude.

Synthetic ethanol is produced from ethylene by catalytic hydration with sulphuric acid and the resulting ester is hydrolysed. The data for synthetic ethanol production have been obtained from industry and are valid for 1995.

LCA results

Ethanol production from renewable raw materials requires very large amounts of energy which are, however, predominantly renewable. In the case of sugar cane, the energy supply was assumed to be self-sufficient and to require only small quantities of fossil energy. The demand for fertiliser, transportation, and machinery is approximately 6 MJ/kg ethanol. The energy demand for grain is lower, owing to the allocation of environmental pollution to associated products (*e.g.* animal feeds), but the production process relies on an external energy supply. For this reason, the amount of fossil energy required rises to about 19 MJ/kg ethanol. Synthetic ethanol production uses crude oil and natural gas as the carbon source. The process steps – refinery, steam cracker for ethylene production and actual synthesis – consume 62 MJ of fossil energy per kg ethanol.

Consumption of renewable energy carriers is rated more favourably than consumption of non-renewable fossil energy. Therefore, in terms of primary energy consumption, despite the higher overall quantities, bioethanol production is superior to synthetic ethanol production.

In terms of CO_2 emissions, biotechnological production has major advantages: bioethanol acts as a CO_2 sink, even more for sugar cane than for grain (Table 4.7).

Table 4.7. **CO_2 emissions from synthetic and biotechnological ethanol production**

Production step	Bioethanol	Bioethanol	Synthetic ethanol
Basis	Sugar cane	Grain	Crude oil/natural gas
Energy supply for ethanol production	Self-sufficient bagasse combustion	Public	Internal/public
Overall production	3.17 kg/kg	1.50 kg/kg	1.88 kg/kg
Bagasse combustion	–2.82 kg/kg		
CO_2 bound up in ethanol (94.5%)	–1.81 kg/kg	–1.81 kg/kg	
Total CO_2 emissions	–1.46 kg/kg	–0.31 kg/kg	1.88 kg/kg

Source: IKP, University of Stuttgart, 1996*a*.

In terms of other emissions into the air, the data are less reliable. For sugar cane, the combustion of bagasse and the cultivation of sugar cane are responsible for emissions into the air. For grain, the sources of emissions are cultivation and process energy. With synthetic ethanol, the emissions result from the production and treatment of the crude oil or natural gas and from the energy required for these processes. For parameters such as sulphur dioxide, bioethanol and synthetic ethanol are in the same range. For particle emissions, sugar cane is at a disadvantage because of the burning off of moisture, while this is not true for grain. Both sugar cane and grain release more nitrogen oxide than the synthetic process.

CONCLUSIONS AND RECOMMENDATIONS FOR FURTHER METHODOLOGICAL WORK

While LCA studies are both highly appropriate and feasible, in principle, for biotechnological products and processes, relatively few are available to date. There are two principal reasons for this. First is the relatively recent appearance of biotechnological processes, compared to chemical ones. Second is the greater methodological difficulty involved in assessing biotechnological processes. In contrast to LCA for classical syntheses, there are considerable procedural differences. Biotechnologically derived products often use renewable raw materials, and this raises questions about assessment of the use of renewable resources, of land use and of CO_2 credits (*i.e.* the CO_2 produced during biotechnological processes as compared to other CO_2 producing processes). In many cases, the baseline data for biotechnological production are inadequate. Access to vital information is impeded because biotechnology companies are often unwilling to release it on the grounds of confidentiality and company strategy.

The advantages of LCA for biotechnological products and processes lie in the possibility of concentrating on those links in the production/consumption chain that are really relevant to determining environmental differences among alternatives. This provides an opportunity to optimise the processes under consideration.

However, only in exceptional cases is sufficient information currently available on mass and energy flows. Process parameters, such as type and amount of emissions into air, water and soil, are not readily available. Furthermore, it is difficult to make generalisations or to apply conclusions from one biotechnological production process to another, because the majority of processes to date are "unique". There are, however, studies which discuss the material and energy flows necessary for the agricultural production of renewable resources. They often concern the use of different raw materials for the same product (ethanol can be made from cane, beet, maize, cellulose, etc.). They show wide country-specific or soil-specific variations and point to dependence on annual crop yields for the raw material in question. Moreover, the data scattering is greater for biotechnological production. Fluctuating yields and holding times of feedstocks and start-up procedures need to be studied over longer periods of time.

In order to compare findings, functional equivalence must be verified. This test has greater significance for many biotechnological or genetically engineered products than for products manufactured by classical methods, not only because of technical issues, but because controversial public discussion can add an ethical dimension. Therefore, the usual procedures for collecting data for LCA studies have to be adapted to the particular requirements of biotechnology. This will require the further development of appropriate methodological tools.

Need for further methodological research at the LCA/biotechnology interface

It is possible to identify a wide range of research topics that might lead to the improvement and wider use of analytical decision-supporting tools such as LCA. This section highlights some that might be given priority (see Annex 4.4 for a comprehensive list).

First might be a holistic approach to harmonising LCA with other methodologies, including "green accounting" and other means of setting goals, and determining the principles for selecting the most appropriate tool or tools.

A simplified approach might involve the development of "quick and easy" techniques that provide less detailed, but nonetheless soundly based, findings which still satisfy stakeholder expectations. Could easily applicable scenario techniques be used to incorporate market or technology changes in the analysis? What is the influence of changing technologies and market shares on the outcome of an LCA?

More work is required on simple decision rules relating, for example, to the definition of system boundaries. This is particularly relevant for biological processes, such as forestry, which may be considered either as part of the environment or as part of the economic system. When considered as part of the economic system, sunlight, CO_2, H_2O, etc., are environmental inputs, but biomass is the input when biological processes are considered as part of the environment. The main question is: Which activities and processes are to be considered part of the production system and which are part of the environment?

Classification

A better understanding of material flows and their relationship to environmental impacts is needed. How should data be sourced and their reliability assessed? Research should be intensified, particularly with regard to:

- the development of classification and characterisation of "land", taking different system boundaries and areas for protection into account;
- the development of classification and characterisation for toxicological impacts, taking different exposure situations into account;
- the development of methods for determining non-toxicological impacts on human health.

Weighting

Since there are ethical and ideological values involved in assessment and since there is unlikely to be a consensus on such values in an open democratic society, it can be expected that several assessment methods and sets of assessment weighting factors will be developed. In order to find out how different groups of people assess different aspects, it may also be useful to use different assessment methods and sets of assessment weighting factors in specific case studies.

It is imperative to evaluate the role of weighting in LCA by:

- developing procedures for weighting, using panel approaches;
- developing monetarised weighting methods, *i.e.* estimating any costs for protecting or repairing the environment, soil remediation, or integrated pollution protection systems;
- evaluating the applicability and acceptability of physical single score methods, which are used where it is useful to compare energy, material use, or production within a single process on an MJ or kg basis.

Other methodological issues

Novel analytical techniques are needed, such as sensitivity analysis and marginal analysis. A sensitivity analysis should include data in the inventory analysis and all quantitative elements of the impact assessment being performed. The results may be further used in different types of statistical analysis to answer questions such as: Is the difference between systems A and B statistically significant?

A marginal analysis provides information on the overall changes that are due to a change in the life cycle. This type of analysis can greatly increase the value of an LCA. By introducing various scenarios (*e.g.* What happens if process A is changed to process B?), a great deal of useful information can be produced which is interesting in connection with an improvement analysis and many other applications of LCA.

Principles and requirements for setting up good databases with appropriate software have to be developed. Advanced modelling and database techniques can be used to represent the time and space pattern of environmental inputs and outputs (*e.g.* coupling LCA with geographical information systems). Harmonisation of data format, etc., is a key element.

Case Study 4.1

GENE TECHNOLOGY TO REDUCE ENVIRONMENTAL POLLUTION

COGNIS GmbH (Henkel) in Germany has published an LCA on detergent proteases which compares the fermentation of genetically modified and unmodified micro-organisms (Bahn and Intemann, 1997).

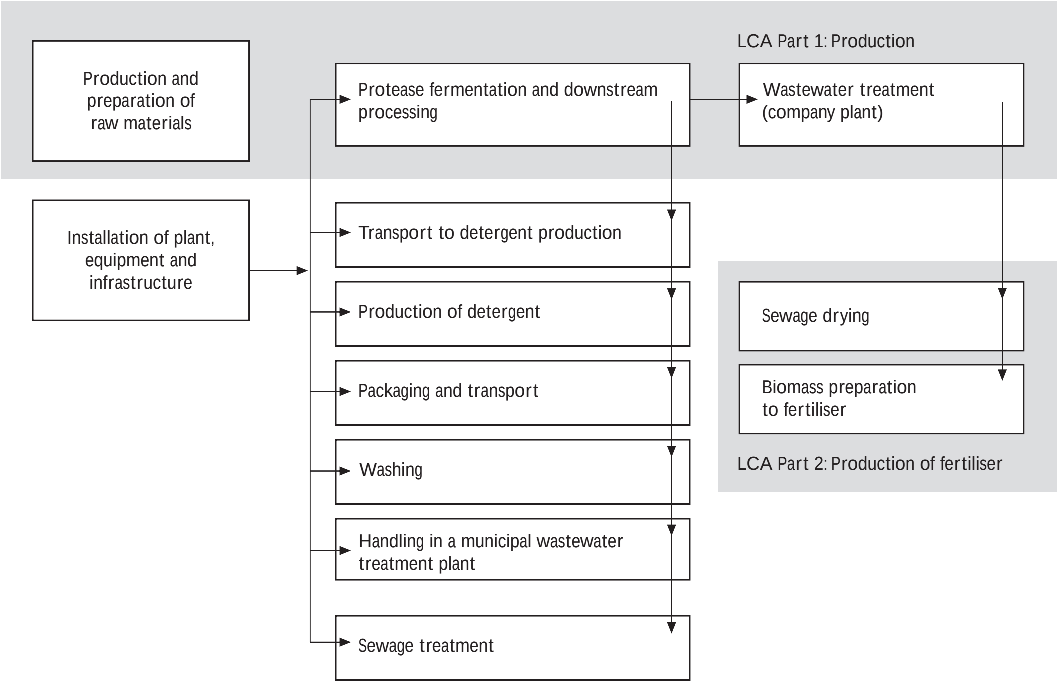
Detergent proteases, which remove protein impurities, are essential components of modern detergents. Owing to their catalytic effect, only low concentrations (0.1-1.0 per cent of proteases are used. Similar washing performance cannot be achieved by substituting other substances or by raising the washing temperature. The micro-organisms used to produce the four types of proteases are as follows:

- P1: Protease produced by a micro-organism that has been optimised by classical selection processes.
- P2 wild: Protease produced by a micro-organism isolated from nature and, compared with the protease of the first generation enzyme, it has a high molar washing capacity.
- P2-140: Protease produced by a genetically modified strain. The gene for second generation protease was incorporated into a proven production strain.
- P2-170: Protease differs from P2-140 by its improved yield in the fermentation process, its technically optimised manufacturing process and its higher enzyme activity in the granulate.

The immediate objective of the LCA was to determine the pollution linked to enzyme production and to reveal any weaknesses in the enzyme production process. A further objective of the LCA was to assess the ecological potential of genetic engineering methods.

The assessment covers not the whole life cycle of detergent proteases but only enzyme production (Figure 4.6), including all processes from production of raw materials to the finished granulate. Consideration is also given to transport of the raw materials used during enzyme production from the

◆ Figure 4.6. ***Protease production, a part of the detergent enzyme LCA***



individual manufacturers to the enzyme producers. No attention was given to buildings, apparatus, etc., as enzyme production is an energy-intensive and mass-intensive process in which the infrastructure plays only a very minor part.

In the cases considered, protease production yields only one useful by-product, an organic fertiliser that is produced from the biomass resulting from protease production. The sludge is first mechanically drained and then dried thermally to achieve a highly nutritive fertiliser.

The enzyme granulates of the two proteases differ by reason of their specific enzymatic activity and by their different washing performance (WP), depending on the degree of soil, washing conditions, and the other detergent ingredients. A purely quantitative comparison would disregard these different properties. For this reason, the average WP, corresponding to 1 kg P1 granulate, average value of six soilings at 30, 45 and 60 °C, was established as the functional unit.

INVENTORY

For the inventory, the input factors used (raw materials, etc.) are usually calculated.

Raw materials

Table 4.8 shows the raw materials that are directly required for the enzyme production. To produce 1 kg P1 granulate requires a total of 3.54 kg raw materials, and the proportion of renewable agricultural raw materials is approximately 50 per cent. To obtain a quantity of P2-140 granulate with an equivalent washing performance, only 2.34 kg are required, so that the raw material demand is reduced by 34 per cent.

Table 4.8. **Raw materials required for the production of P1, P2 wild, P2-140 and P2-170**

	Unit	P1	P2 wild	P2-140	P2-170
Agricultural raw materials	kg/WP*	1.83	24.64	1.76	1.56
Mineral raw materials	kg/WP*	1.17		0.44	0.38
Fossil raw materials	kg/WP*	0.54		0.14	0.14

WP* = enzyme quantity whose WP corresponds to 1 kg P1 granulate.

Energy demand

When analysing energy demand, it is necessary to distinguish between process energy and inherent energy. Process energy includes the total amount of primary energy that is required in the form of renewable or fossil energy and is ultimately "consumed". Inherent energy is the energy that is chemically bound in the enzyme granulate or fertiliser. Inherent energy is not permanently lost, but can, under certain circumstances, be recovered. Table 4.9 summarises the energy consumption aggregated over the whole production chain.

A change from P1 production, optimised by means of conventional mutagenesis, to production of P2-140 by means of genetic engineering, reduces the demand for process energy by 60 per cent, from 131 MJ/WP to 52 MJ/WP. Additional ecological optimisation of enzyme production can be achieved by changing from P2-140 to P2-170.

The production of the Henkel Group's annual requirements of the current P2-140 granulate, instead of the earlier washing performance equivalent amount of P1 granulate, results in primary energy savings of approximately 420 000 GJ. This corresponds to the annual primary energy consumption required for the laundry purposes of about 170 000 households or 380 000 persons.

Table 4.9. **Aggregate consumption of primary energy for the whole enzyme production chain of the detergent proteases P1, P2 wild, P2-140 and P2-170**

	Unit	P1	P2 wild	P2-140	P2-170
Process energy					
Energy (fossil)	MJ/WP*	102	397	41	31
Energy (renewable)	MJ/WP*	29	182	11	8
Inherent energy					
Energy (fossil)	MJ/WP*	6	3	3	2
Energy (renewable)	MJ/WP*	17	6	6	5

WP* = enzyme quantity whose WP corresponds to 1 kg P1 granulate.

EMISSIONS

In addition to the input factors, emissions also have to be calculated. Table 4.10 summarises the aggregate emissions of the various detergent proteases over the total production chains.

Table 4.10. **Aggregate emissions for the total enzyme production chains of detergent proteases P1, P2 wild, P2-140 and P2-170**

	Unit	P1	P2 wild	P2-140	P2-170
Atmospheric pollution					
Total carbon dioxide	g/WP*	8 507	37 376	3 422	2 571
– From renewable raw materials	g/WP*	1 548	12 745	849	614
– From fossil raw materials	g/WP*	6 959	24 632	2 572	1.957
Hydrocarbons	g/WP*	67	331	36	27
Sulphur oxides	g/WP*	60	234	25	19
Nitrogen oxides	g/WP*	49	150	15	12
Dusts	g/WP*	24	72	7	5
Carbon monoxide	g/WP*	14	21	2	2
Wastewater pollution					
Chemical oxygen demand	g/WP*	158	1 008	77	57
Biological oxygen demand	g/WP*	7	56	4	3
Waste					
Organic waste	g/WP*	1 033	3 147	313	237
Slag/ashes	g/WP*	98	263	26	19

WP* = amount of granulate whose washing performance corresponds to 1 kg P1 granulate.

CARBON DIOXIDE EMISSIONS FROM FOSSIL AND RENEWABLE RAW MATERIALS

For CO_2 emissions, a distinction is made between emissions arising from the use of renewable raw materials and from the use of fossil energy, mainly to produce electricity and heating. As a result, in the case of P1 granulate, 6.96 kg CO_2 is released and in that of P2-140 granulate, 2.57 kg, in each case relative to the washing performance of 1 kg P300. A considerable amount of CO_2 (*e.g.* 1.55 kg CO_2 per kg P1 granulate = 20 per cent of total CO_2 emission) is also formed by the biological degradation of renewable raw materials during fermentation and aerobic wastewater purification.

In terms of the company's annual demand, application of the new enzyme produced with recombinant organisms made it possible to reduce the annual emissions by approximately 30 000 tonnes of CO_2, 170 tonnes of carbon, and 190 tonnes of sulphur oxide.

IMPACT ASSESSMENT

In the case of assessments based on environmental criteria, emission data are compiled according to their connection with selected environmental impacts (Table 4.11). If possible, the various emissions are weighted by scientifically sound factors – published by the German *Umweltbundesamt* (environmental authority) – in order to take account of the various types of impacts.

Table 4.11. **Assessment of emissions and waste arising from the production of detergent proteases on the basis of environmental criteria**

	CO_2 factor	Unit	P1	P2 wild	P2-140	P2-170
Global warming						
Carbon dioxide	1	g CO_2/WP*	8 507	37 376	3 422	2 571
Hydrocarbons	20.5	g CO_2/WP*	1 383	6 778	729	556
	SO_2 factor	Unit	P1	P2 wild	P2-140	P2-170
Acid rain						
Sulphur dioxide	1	g SO_2/WP*	60	234	25	19
Nitrogen oxide	0.7	g SO_2/WP*	35	105	11	8
		Unit	P1	P2 wild	P2-140	P2-170
Smog formation						
Hydrocarbons		g/WP*	67	331	36	27
Dusts		g/WP*	24	72	7	5
Carbon monoxide		g/WP*	14	21	2	2
	PO_4 factor	Unit	P1	P2 wild	P2-140	P2-170
Oxygen consumption						
Ammonia	0.32	g/PO_4/WP*	6	62	4	3
Nitrogen oxide	0.13	g/PO_4/WP*	6	20	2	1
CSB	0.02	g/PO_4/WP*	3	22	2	1
		Unit	P1	P2 wild	P2-140	P2-170
Waste						
High pollution		g/WP*	1 131	3 410	338	256
Low pollution		g/WP*	3	5	1	1

WP* = amount of granulate whose washing performance corresponds to that of 1 kg P1 granulate.

Within the framework of this LCA, atmospheric emissions were assessed in terms of impact on global warming, development of acid rain, and smog formation. Aquatic emissions were assessed according to the yield of nutrients in water and related oxygen consumption. For waste, a distinction was made between types with a low pollution effect and those with a high pollution effect. The impact assessments clearly confirm the general claim that the use of a recombinant strain can reduce the consumption of energy and resources and the pollution in the form of emissions by a factor of 3-4.

Case Study 4.2

ETHANOL PRODUCTION

DEFINITION OF GOAL

This case study compares the production of bioethanol with synthetically produced ethanol. The goal of the study was to establish the feasibility, in principle, of an LCA for products produced by biotechnological processes, along with a description of the system and the boundary conditions as well as an interpretation of the findings. The elements of the study are as follows:

- The inventory for ethanol produced by biotechnological processes is assessed and compared with synthetically produced ethanol.
- The baseline data for ethanol produced by biotechnological processes are very lean and, depending on the basic raw materials used and their sources, subject to fluctuations. For this reason, the interpretation of the findings reflects trends.
- The study is confined to the production of ethanol. It can be assumed that the processes compared result in equifunctional products and that both consumption and disposal take place in the same way.
- Assertions are made about the environmental parameters *utilisation of energy resources* and *selected emissions into the air*. Only a more comprehensive study could adequately address the factor ''land use'', which is important in connection with renewable raw materials.
- It is intended to show what potential for reducing pollution can be inferred from this succinct case study.

DESCRIPTION OF THE SYSTEM AND SCOPE OF THE STUDY

Table 4.12 shows the physical properties of ethanol. In principle, no variations in properties can be gleaned from the production route.

Table 4.12. **Physical properties of ethanol**

Size	Value
Empirical formula	C_2H_5OH
Relative molar mass	46 kg/kmol
Carbon content	52.2% by weight
Carbon content calculated as CO_2 for 94.5% ethanol	1.81 kg
Calorific value	26.8 MJ/kg
Mass density	793 kg/m^3

BIOTECHNOLOGICAL PRODUCTION OF ETHANOL FROM SUGAR CANE

The production route can be divided into the following steps: fermentation of the carbon source, biotechnological conversion into ethanol, and distillation of ethanol. Carbohydrates (glucose and sucrose), which are derived, for instance, from sugar cane, sugar beet, grain, root crops, wood and waste liquor, are the carbon source. Two cases for bioethanol are presented: production using sugar cane and production using grain.

In autumn 1996, the *Institut für Kunststoffprüfung und Kunststoffkunde* (IKP) carried out the research for this study (IKP University of Stuttgart, 1996*a*), which is based on both the literature (Crueger and Crueger, 1990; Ward, 1994; Dellweg, 1987; Osteroth, 1992; ETH Zurich and Labor für Energiesysteme,

1994) and on oral communications concerning sugar cane cultivation and its processing into ethanol. The production location is Brazil. The following aspects should be borne in mind:

– The fields are often burned before harvest, as this makes harvesting easier. This causes considerable emissions. Since this practice is being abandoned, these emissions have been disregarded.

– The demand for primary energy from renewable raw materials was confined to sugar cane. Any other biomass produced in the cultivation was disregarded.

– The use of farm vehicles both during the growth period and during the harvest was estimated, but not the necessary infrastructure.

– It is to be expected that emissions will develop, particularly over fertilised fields. No information was available on this point. Also, the study disregarded groundwater pollution caused by fertilisers.

The boundary conditions for sugar cane cultivation are presented in Table 4.13 and the inventory of processes in Table 4.14.

Table 4.13. **Baseline data for the LCA study**

Parameters for sugar cane cultivation	Value/unit
Use of fertiliser	1.6 MJ/kg sugar cane
Machines/transportation:	
Fuel consumption	0.067 l/kg sugar cane
Other machines	0.095 kWh/kg sugar cane

Source: Bernhardt and Menrad, 1979.

Table 4.14. **Inventory of the processes involved in sugar cane cultivation**

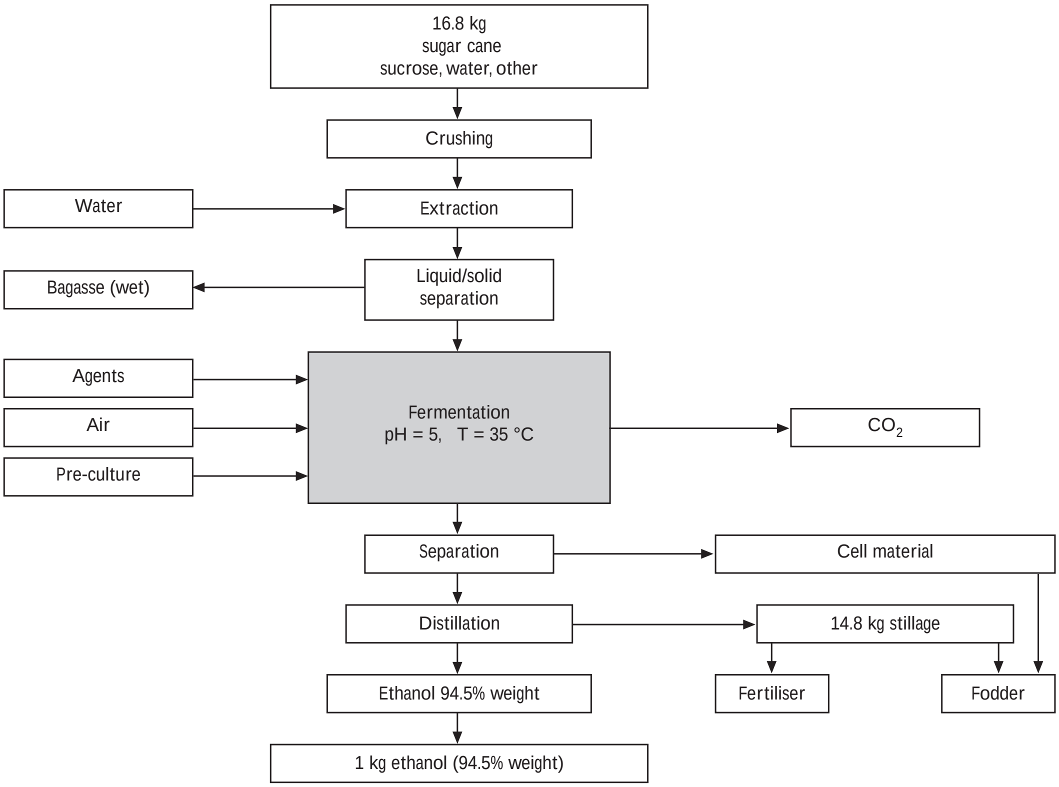
Process	Parameter
Use of fertiliser	Calculated as nitrogen fertiliser
Machines/transportation	Farm machines running on diesel, calculated as diesel lorry transportation
Other machines	Power consumption

Ethanol is produced with the use of yeast. The procedure for producing ethanol from sugar cane is as follows. After the sugar cane has been crushed (tube mills) it is extracted with water. The sucrose yield is 99 per cent. The bagasse is then separated from the sugar cane liquor feedstock. In the fermentation step (slightly acid medium, pH = 5, t = 28 °C), the sucrose is converted, by the yeast, into ethanol, carbon dioxide, and, in small quantities, into glycerine. The separation step separates the liquid from the biomass, which is returned to the fermentor. In the distillation stage, ethanol with a 94.5 per cent degree of purity is produced. The resulting stillage can be used as fertiliser or fodder.

The analysis of mass flow in Figure 4.7 begins with harvested sugar cane and ends with ethanol. The following parameters should be considered when an LCA is made.

Burning the bagasse means that, from crushing the sugar cane to obtaining 94.5 per cent ethanol, ethanol production is, from the point of view of energy, self-sufficient. Credits, *e.g.* for supplying energy to third parties, were not included. With the exception of CO_2, the emissions from the bagasse combustion are calculated using emission factors for wood firing according to the eco-inventory for energy systems (ETH Zurich and Labor für Energiesysteme, 1994). Specific information on bagasse combustion was not available.

◆ Figure 4.7. ***Mass flow for the biotechnological production of ethanol***



Source: IKP, University of Stuttgart, 1996*a*.

The CO_2 mass taken from the environment where sugar cane is cultivated has not been taken into account. Only the amount bound up in ethanol, *i.e.* 1.81 kg CO_2/kg ethanol (94.5 per cent), is credited to the product.

The production of 1 kg of ethanol gives rise to approximately 14.8 l stillage, which is released into water or deposited as fertiliser. It may also be further processed into fodder. It was assumed that the product is used, but no allocation of environmental data for this product was made.

Because insufficient information was available for the areas of water and soil pollution, the case study does not address these environmental parameters.

The baseline data were taken from studies (Morris and Ahmed, 1992) and (Lorenz and Morris, 1995). The energy data for the "industrial average" case were linked to corresponding processes of the GaBi Progress 2.0 database (IKP University of Stuttgart, 1996*b*). The essential differences are:

- fertilisation and irrigation require more energy than sugar cane cultivation;
- process energy for ethanol production is covered by the public energy supply or by on-site steam production.

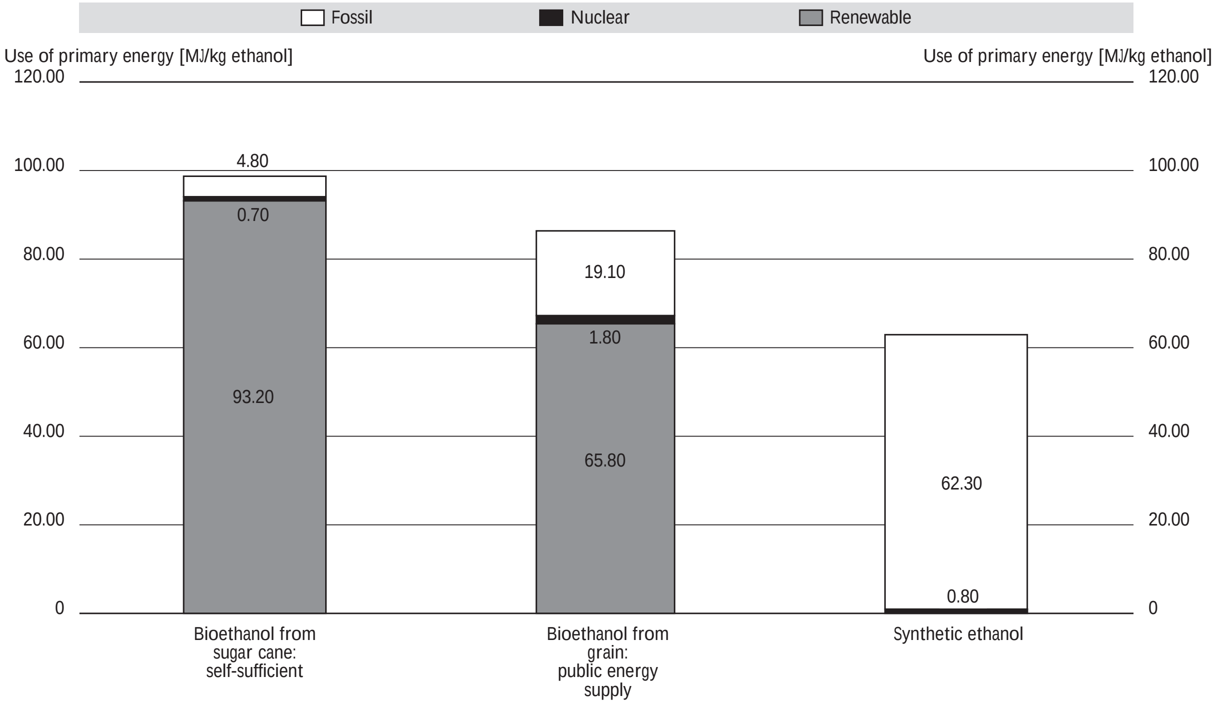
Data for ethanol produced from grain and sugar cane were compared with the values documented in other studies, *e.g.* Parisi (1983), which gives a comprehensive survey of studies on ethanol production from sugar cane, sugar beet, grain and other raw materials. They agree within a certain scatter.

Synthetic ethanol is produced from ethylene by catalytic hydration. Direct hydration employs sulphuric acid. The resulting ester is hydrolysed. The data for synthetic ethanol production have been obtained from industry and are valid for 1995 (IKP University of Stuttgart, 1996*b*).

RESULTS

With due observance of the boundary conditions, the findings can be evaluated to pinpoint trends. The results depicted in Figure 4.8 show the primary energy demand. The energy assimilated from sugar cane or grain via the renewable energy source (solar energy) is designated as "renewable". The other essential energy forms are the fossil energy carriers, crude oil and natural gas.

◆ Figure 4.8. ***Primary energy demand for biotechnological and synthetic ethanol production***



Source: Author.

Ethanol production from renewable raw materials requires very high amounts of energy which are, however, predominantly renewable. In the case of sugar cane, it was assumed that the energy supply was self-sufficient and required only small quantities of fossil energy. The demand for fertiliser, transportation and machines amounts to approximately 6 MJ/kg ethanol. The energy demand for grain is lower on the whole, owing to the allocation of environmental pollution to related associated products, and reliance on an external energy supply. For this reason, the amount of fossil energy required rises to about 19 MJ/kg ethanol.

Synthetic ethanol production uses crude oil and natural gas as the carbon source. The process steps – refinery, steam cracker for ethylene production and actual synthesis – consume 62 MJ/kg ethanol of fossil energy.

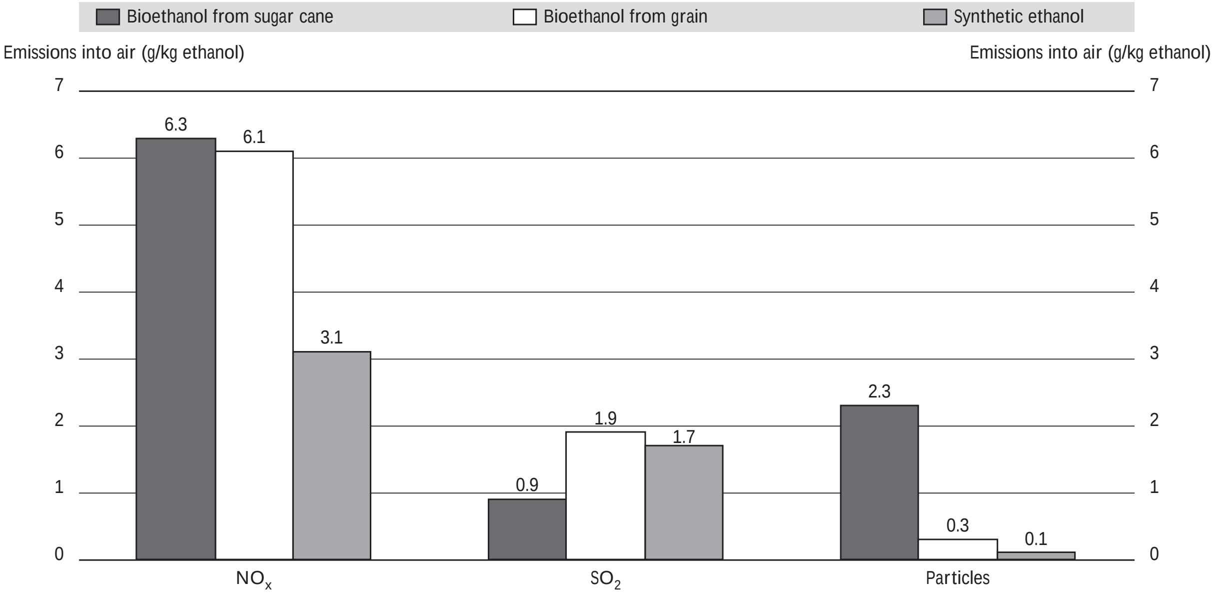
Consumption of renewable energy carriers is rated more favourably than consumption of non-renewable fossil energy. Therefore, in terms of primary energy consumption, despite the higher values, bioethanol production is superior to synthetic ethanol production.

When considering the CO_2 emissions, even taking oversimplified assumptions into account, biotechnological production has advantages. Bioethanol acts as a CO_2 sink, even more in the case of sugar cane than in that of grain.

The burning off of damp, renewable raw materials causes distinctly higher carbon monoxide (CO) emissions. For this environmental parameter, which is admittedly of local significance, bioethanol with 27 g/kg clearly has a higher value than synthetic ethanol (0.4 g/kg).

In terms of other emissions into the air, the data are less clear-cut. A selection of emissions is given in Figure 4.9.

◆ Figure 4.9. ***Emissions into the air caused by synthetic and biotechnological ethanol production***



Source: Author.

For sugar cane, the combustion of bagasse and the cultivation of sugar cane are responsible for emissions into the air. For grain, the sources of emissions are cultivation and process energy. With synthetic ethanol, the emissions result from the production and treatment of the crude oil or natural gas and from the energy required for these processes. For parameters such as sulphur dioxide, bioethanol and synthetic ethanol are in the same range. For particle emissions, sugar cane is at a disadvantage because of the burning off of moisture (as for CO emissions), but this is not true for grain. Both sugar cane and grain release more nitrogen oxide than the synthetic process, owing to the availability of process energy.

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PUBLIC ATTITUDES AND EDUCATION*

- **There is a need to communicate to the public and to their government representatives the value of clean technology and the role of biotechnology for achieving industrial sustainability.**
- **There are significant differences in public awareness and attitudes towards biotechnology from one country to another.**
- **Active measures targeted at opinion formers in the media and non-technical communities will be required to promote wider understanding of biotechnology and to reach different constituencies.**
- **There is a need for more and better information on public attitudes towards products of biotechnology.**
- **Educational programmes need to be devised that will underpin scientific understanding at all levels.**

Public attitudes and public pressure are among the most important drivers for the introduction of clean products and processes, including those derived from modern biotechnology. It is therefore fitting that this report should include a discussion of the general public's views of clean products and processes and their relation to modern biotechnology and of the policies that may be appropriate to encourage better public understanding of the issues involved.

During the 1960s, increasing concern over the environment centred primarily on issues such as source of pollution, dissemination of pesticides, air pollution in particular cities, and incidents of oil pollution at sea. Since then, concerns have broadened, partly because of the increasing number of industrialising countries. They have also become systemic, and now focus on the integrity of the planetary ecosystem.

Efforts to rethink and refashion industrial processes in this wider perspective must find support in many different ways and in disparate sectors of society. They must also find acceptance among peoples throughout the world.

CAN BIOTECHNOLOGY HELP?

Chapters 1, 2, 3 and 4 have amply demonstrated that biotechnology has the potential to provide the basis for such a radically new approach. At its core would be the principle of working in harmony, rather than in conflict, with the natural world. Biotechnological and other solutions could supplant existing technologies that pollute the biosphere and/or deplete finite resources. A strategy that reduces the impact of such technologies clearly improves, rather than degrades, the quality of the natural environment.

There is also a widely held (though not unanimous) view among the scientific community that the genetic modifications that are part of modern biotechnology are not so radically new that they bring unprecedented and unfathomable uncertainties as to their consequences. This is why regulatory authorities, having treated the products of genetic manipulation as distinctively different from other products for several years, are being urged by scientists to move towards regulation focused on products rather than on the methods by which they are made.

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* This chapter was drafted under the responsibility of Dr. B. Dixon (UK).

For these reasons, the concept of clean technology based on biological approaches may attract public support. However, the public still has some concerns about modern biotechnology particularly as it is applied to the consumption of food produced using recombinant organisms. In some countries, this has led to public demands for labelling of foods and other products. The public is most likely to be receptive to biotechnology when it is used to improve human health or to reduce the environmental impact of industrial processes.

Box 5.1. **Environmentalists welcome bioethanol**

Iogen is a biotechnology company in Ottawa which makes enzymes to digest wood waste and crop residues to make sugar, which is then refined into ethanol; Petro-Canada is one of Canada's largest oil companies. When Petro-Canada recently announced it would put money and refining experience into a venture with Iogen, including building a $15 million to $30 million ethanol test plant next year, co-funding for R&D and a licensing option to build full-scale ethanol refineries, environmental groups reacted very positively.

A Sierra Club spokesperson declared, "It spells the beginning of a new energy industry. Petro-Can has made a wise investment. I hope they make lots of money, and I hope Iogen makes lots of money." The Sierra Club campaigns against fuels that create "greenhouse" gases, which cause global warming. "It's very exciting", said an energy analyst with Energy Probe, a Toronto-based group which supports alternative energy sources. "We've been part of the fan club of this cellulose-based ethanol for a long time." The Pembina Institute, another group that focuses on the global warming issue, stated, "We haven't had a lot of good news stories on climate change in Canada. This is one. Even major oil companies can see the economic advantage in greenhouse-gas emission reductions. It won't be the solution, but it definitely will contribute, along with a lot of other things such as increased fuel efficiency."

Both companies say the high-tech process – which will use bioengineered enzymes to convert low-cost cellulose into ethanol – could give them a commanding lead in the race to replace fossil fuels in Canada's transportation sector.

Moves towards the development of clean technology, based on biological approaches, are not intrinsically novel. They do not therefore carry the same degree of inherent unpredictability and possible unforeseen danger that has characterised many other developments in the past. These features of clean technology, or biotechnology, certainly do not guarantee public acceptance. Nor should they. However, there is a considerable difference between the harnessing of enzymic, microbial and other processes that already fashion the biosphere, and the introduction of a technology founded upon techniques which mark a sharp departure from what has been done before.

However, several important qualifications need to be taken into account, not least in measures to promote public understanding of biotechnology. Just as bioremediation, for example, should not be promoted as *always* being the most desirable approach to environmental clean-up and waste disposal, so biotechnology in general should not be misrepresented or over-sold as a universal panacea. There will be occasions when biotechnology does *not* offer the most prudent solution.

Nevertheless, one implication of this report's scientific, technological and economic assessment is that an overall trend towards biotechnological approaches is desirable from the perspective of the public as well. This trend reflects not only contemporary technical innovation but also imperatives to conserve energy and materials and reduce environmental pollution. It may in fact gain greater public support than equivalent industrial changes in the past.

To give an example of how the climate of opinion can affect society's use of technology, both California and the United Kingdom have already seen the force of public opinion behind demands for lead-free and otherwise environmentally more acceptable gasoline. With the growing realisation that alternative pathways of industrial development are possible, there could be increasing calls for the introduction of many other cleaner products and processes.

PUBLIC ATTITUDES TO BIOTECHNOLOGY

As with any other technology, perceptions of biotechnology are influenced (sometimes very strongly) by information disseminated via the media and other channels. Public information, or misinformation, about the complex links between technology, regulation, and political action are thus of crucial importance for public endorsement or rejection of new technical developments. More than ever before, such innovations can proceed only insofar as scientists and their regulators enjoy public trust. Politicians, who set the agendas, guidelines and laws within which the regulators operate, are heavily influenced by public opinion/debate, and in particular by the way in which it is reflected in the media.

Biotechnology applied to the development of ecologically prudent industrial processes may appeal to young people who, throughout the world today, are strongly motivated by concern both for the environment and for less privileged regions of the world. As outlined below, there is also evidence of greater confidence in biotechnology than is suggested by the efforts of those who oppose it.

There is little or no specific quantitative evidence on public perceptions of biotechnology applied to cleaner industrial processes. Soundings can only be extrapolated, therefore, from research into attitudes about biotechnology in general. For example, a recent survey of New Jersey residents (Hallman, 1996) revealed that over two-thirds believed that genetic engineering would improve the quality of life. Likewise, a 1991 "Eurobarometer" survey of 13 000 European Union citizens (International Research Associates, 1991), showed that over three out of four agreed that "science and technology are making our lives healthier, easier and more comfortable". Only 8 per cent disagreed with this statement. With the exception of applications involving farm animals, there was also strong backing for specific uses of biotechnology.

A strong 87 per cent of respondents supported research into "micro-organisms used to break down sewage and other waste products and turn them into materials harmless in the soil". Very similar findings were reported for Japan (Macer, 1992) on both the general acceptability of genetic engineering and its application to environmental improvement.

The latest Eurobarometer survey on various technologies, conducted in 1996, covered some 16 000 people (an average of 1 000 per country). Although it did not specifically explore public attitudes towards environmental aspects, the report (INRA, 1997) concluded that Europeans generally take an optimistic view of developments in modern biotechnology. However, the authors also warned that "this is not blind optimism: they may emphasise the benefits of certain areas of research, but they also warn of potential risks".

Another indication that the results of surveys of this sort should be treated with caution comes from contrasts between the report and an account of the same data by a group closely associated with the Eurobarometer exercise (European Public Concerted Action Group, 1997). In contrast with the cautiously optimistic verdict of the INRA report, this group concluded that "many Europeans are uneasy about modern biotechnology, particularly about new genetic technologies". Moreover, whereas the former stated that the results were very similar to those of the 1991 Eurobarometer survey, the latter concluded that optimism about the contribution of biotechnology declined over those five years.

According to other findings of the 1996 Eurobarometer study, some 80 per cent of Europeans believe that applications such as the production of medicines and the development of genetic tests to detect diseases will benefit society, 69 per cent considered it beneficial to introduce pest-resistant genes into crop plants, while only 54 per cent thought that the use of modern biotechnology in food production was beneficial.

Participants were generally most optimistic about telecommunications, information technology, solar energy, and new materials. Fewer people expected benefits from biotechnology, space exploration, and genetic engineering. Nevertheless, this did not mean that they were pessimistic about these fields. Many of those surveyed had no opinion.

KNOWLEDGE AND ATTITUDE

Support for modern biotechnology increased with income, level of education, and objective knowledge of the subject (also assessed in the Eurobarometer questionnaires). The percentage of optimists was as high as 67 per cent for those respondents who correctly answered all ten factual questions, as compared with only 17 per cent of those who answered them all incorrectly. A response category which declined steeply with greater knowledge was the ''don't knows''.

Reactions regarding the moral acceptability of various uses of biotechnology were strong. Participants largely felt that genetic tests to detect disease (74 per cent) and the production of medicines and vaccines by genetic engineering (70 per cent) were morally acceptable, but only a minority (40 per cent) endorsed the development of genetically modified animals for laboratory research or the use of genetic engineering to make organs for human transplants (36 per cent).

Multiple regression analysis showed that while the specific biotechnology application, and its moral acceptability, were strong predictors of support, risk *per se* was a poor predictor. This may indicate a mismatch between the traditional concern of regulators with issues of risk and safety and that of the public, which now centres on moral acceptability (European Public Concerted Action Group, 1997).

These data and those of other surveys do not support the idea, often heard, that there is strong public opposition to biotechnology and/or genetic engineering. Nor do they indicate widespread endorsement. They do suggest, however, that it is simplistic and misleading to measure the temperature of public opinion along a single scale from enthusiasm to hostility. One of the single most telling results in the 1993 Eurobarometer survey (INRA, 1993) was that, of all the countries studied, Denmark had both the strongest support for biotechnology and the highest perception of risk. In other words, it is possible to combine high regard for the achievements of science, in areas such as medicine, agriculture and environmental improvement, with concern about potentially adverse consequences of new technology.

Further evidence comes from a survey conducted by Evans and Durant (1995), who measured general attitudes in Britain by asking nine questions, ranging from whether scientists can be trusted to whether science is changing our lives too quickly. The results showed a generally positive view of science: 70 per cent of respondents said they believed science and technology are making our lives healthier and more comfortable, and 80 per cent backed government support for ''research which advances the frontiers of knowledge''. The pattern was not uniform, however, as some respondents agreed with both positive and negative statements.

To determine whether respondents' overall view of science was reflected in their opinions on individual areas of research, Evans and Durant used further sets of questions. The specific topics included creating new forms of animal life and finding a cure for cancer. Here, correlations were at best moderate: highest for useful and basic science and weakest for morally contentious research. In other words, participants' responses to questions about their general attitude towards science and technology did not permit accurate predictions of how they felt about particular types of research.

A third analysis compared respondents' attitudes to science with their factual knowledge, evaluated on the basis of their response to various statements about the natural and medical sciences. Here, Evans and Durant discovered that although there was a significant correlation between attitude and knowledge, its strength varied considerably. Factual knowledge was moderately well correlated with participants' general attitudes and their attitudes towards useful and basic research. On the other hand, knowledge was almost wholly unrelated to attitudes about research that was not considered useful. Moreover, there was a strong *negative* association between knowledge and support for research which could be seen as morally contentious.

REGULATIONS AND NON-GOVERNMENTAL ORGANISATIONS

Of the six industrial sectors reviewed in this report (Chapter 2), the food sector has raised problems in some countries in terms of public acceptance of food manufactured with the use of recombinant organisms. While the focus of this report is clearly not on genetically modified foods but on cleaner food processing technologies which might make use of methods derived from genetic engineering, it cannot be excluded that the some elements of the public might react to cleaner processing technologies based on genetic engineering as they might to genetically modified foods.

For many individuals, the key issue will not be knowledge or technical understanding but confidence in the regulatory system, as for the safety of air travel, for example. Indeed, public trust is never likely to be secured by the provision of information alone. Equally important are factors such as the transparency of decision making about new technology, the assessment of risk, and the regulation and monitoring of both research and its practical applications.

Regulation and legislation for biotechnology may reflect or anticipate public concerns, either actual or perceived. There is a continuous interplay, through the political process, between public attitudes and the regulation of biotechnology.

Labelling of food products is one significant issue of concern to the public that has yet to be resolved. In most cases, the approach is the same as for safety; special labelling is not required unless a product of genetic manipulation is substantially different from the traditional product it resembles.

There are a number of non-governmental organisations (NGOs) that influence public policy on the use of recombinant organisms. Most of these focus primarily on medical and agricultural applications using plants and animals, but their activities also have an impact on food processing using micro-organisms in the products. Besides the OECD, the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) have also addressed food biotechnology safety issues, with joint expert consultations in l990 and l996. The most recent FAO/WHO report provides a mainstream view of food safety issues but does not deal with environmental issues, incidental residues from processing aids, or labelling (FAO, 1996).

Several industry-backed organisations are also active on behalf of food biotechnology. The Biotechnology Industry Organization is a United States-based advocacy group with a food and agricultural section. The International Food Information Council, also located in the United States, is a non-profit educational foundation that provides educational programmes on the benefits of food biotechnology. The Enzyme Technical Association (ETA) is a group of enzyme companies based in the United States whose activities include interaction with US authorities regarding the safety of food enzymes derived from recombinant organisms. The Association of Microbial Food Enzyme Producers is a group of enzyme companies based in Europe, with activities similar to those of the ETA.

In addition, a number of consumer advocacy organisations campaign against certain aspects of food biotechnology. The Council for Responsible Genetics and the Foundation for Economic Trends are two of many such US organisations, while Greenpeace and Friends of the Earth are especially active in Europe. Most of these groups are particularly concerned with plant, animal and agricultural issues, but the German chapter of Friends of the Earth has focused specifically on recombinant enzymes used as processing aids.

There are also groups that try to maintain a neutral position. The International Food Biotechnology Council used industry funding but independent experts to prepare a l990 report on scientific criteria for the safety of recombinant foods. The National Center for Genome Resources is a non-profit organisation based in the United States that sponsors a Genetics and Public Issues educational programme covering such foods. SustainAbility is a London-based group that provides independent verification of companies' claims about their environmental performances.

VARIATIONS FROM COUNTRY TO COUNTRY

There is considerable variation in attitude from country to country, as illustrated in the European Commission's Eurobarometer survey of 1996 (International Research Associates, 1997). Whereas 57 per cent of Italians and 56 per cent of Spaniards considered that biotechnology and genetic engineering will improve the quality of life over the next 20 years, only 28 per cent of Austrians and 36 per cent of Germans expressed such confidence. Similar changes in attitude have taken place over the years. For example, optimism towards biotechnology in the Netherlands declined between 1991 and 1993, but returned to the 1991 level by 1996. On the other hand, the level of optimism in Greece continued to fall over the same period.

Consumer awareness of biotechnology varies greatly by country. Austria, Denmark, Germany, and Japan seem to be most aware, while Greece, Italy, and Spain are least aware. The United States and Canada fall somewhere in between, with awareness in the United States declining somewhat between 1992 and 1996 (Hoban, 1997).

Consumer acceptance of food biotechnology also varies, but with a different pattern. The US market has been the most studied, with several surveys consistently showing two-thirds to three-quarters of consumers supporting biotechnology and willing to accept biotechnology food products. Australia, Canada, Japan, and New Zealand have reported similar results. In Europe, however, less than one-third of consumers in Austria and Germany were willing to accept plant biotechnology food products. Consumers in the Netherlands and Portugal were similar to US consumers, while those in other European countries fell somewhere in between (Macer, 1992; Hoban, 1996*b*, 1997; Decima Research, 1996).

Consumers appear to base their acceptance on their perception of risk/benefit. For example, genetic engineering in animals is considered more dangerous than in plants, and medical applications are considered more beneficial than recombinant food. US surveys in 1992 and 1994 showed that the use of biotechnology for human medicines and protection of crops against insect attack was most acceptable, while its use for larger sport fish and food ingredients attracted least support. About equal numbers of respondents found food ingredients made by biotechnology acceptable, unacceptable and neutral (Hoban, 1996*b*).

A 1995 survey of Japanese consumers gave similar results. "Crop plants that reduce the need for pesticides" and "human insulin or other medicines" were most acceptable, and "larger, faster-growing fish" and "food ingredients, such as flavourings" were least acceptable. "Enzymes used in food production" fell in between, with about 40 per cent finding them acceptable, 20 per cent unacceptable and 40 per cent neutral (Hoban, 1996*a*).

The greatest consistency in survey results concerns labelling. Regardless of their awareness or acceptance, consumers in many countries want obligatory labelling of recombinant food products. Typical results come from one regional US study which reported 85 per cent of consumers in favour of mandatory labelling, even though only 58 per cent said they would look for the information or use it when deciding what to purchase (Hallman and Metcalfe, 1993). The desire for labelling may reflect a lack of education about the nature of recombinant organisms. In Canada, for example, consumer associations and local grocery industry groups, which initially favoured labelling, no longer support mandatory labelling as the best approach.

ATTITUDES REGARDING THE ENVIRONMENT

Very few surveys have specifically explored public views on the environmental aspects of biotechnology. A preliminary study conducted in Canada in 1996 focused exclusively on environmental applications. It evaluated attitudes of Canadians via a series of five focus groups conducted across the country. Given a brief introduction to specific environmental applications of biotechnology, participants were generally supportive, particularly when links were made to familiar technologies, *e.g.* composting and production of biofuels. Participants also endorsed biotechnology applications as long as they were kept informed of the benefits and risks. More specifically, support for a variety of environmental applications ranged from 75 per cent for use of biosensors, 79 per cent for production of specialty chemicals, and 86 per cent for biofuels. Environment and health applications of biotechnology were considered a higher priority than food production (McIntyre, 1996).

Another study focused on different potential applications of genetic engineering (Martin and Tait, 1992). The study evaluated attitudes of a UK population sample that included people, chosen at random from electoral registers, who lived in two parts of the country where recombinant organisms had been released, members of Friends of the Earth and other "green" lobby groups, and non-technical staff of companies involved in biotechnology.

Even with a sample of this composition, support for the use of genetic manipulation for environmental decontamination was as strong as for its use in medicine. Some 65 per cent of respondents were "comfortable" with the idea of deploying recombinant organisms to clean up oil slicks and to detoxify industrial waste. This compared with 59 per cent in the case of medical research and 57 per cent in the case of "making medicines".

Martin and Tait drew attention to the unexpected diversity of opinion reflected in these overall percentages when they broke their sample down into its constituent sub-groups. Even areas such as improving crop yields and making medicines, which are not normally considered to be controversial, showed wide variations in response. However, the range of opinion among those who were comfortable with the idea of using genetic manipulation for the two types of environmental decontamination was among the narrowest of all.

Another type of evidence comes from that part of Europe which has seen strong antagonism towards gene technology, the former West Germany. Opposition has abated over the past five to ten years, and Radkau (1995) has attributed this in part to changes associated with German reunification. Not only did the great economic and social problems arising from reunification divert attention from the alleged dangers of gene technology, allegations concerning these hazards were suddenly overshadowed by the emerging recognition of the scale of industrial pollution in East Germany and other eastern countries.

SUSTAINABILITY AND THE PUBLIC MOOD

The definitions and goals of sustainability are discussed in Chapter 1. Already three decades ago, Ward (1966) borrowed Buckminster Fuller's analogy to argue that:

> *... the most rational way of considering the whole human race today is to see it as the ship's crew of a single space ship on which all of us, with a remarkable combination of security and vulnerability, are making our pilgrimage through infinity. ... This space voyage is totally precarious. We depend upon a little envelope of soil and a rather larger envelope of atmosphere for life itself. And both can be contaminated and destroyed.*

Concerns regarding pollution and conservation, which arose during the 1960s and 1970s, led to individual ameliorative measures. However, the subsequent emergence of modern biotechnology raises the possibility of a more profound alteration of the relationship between industry and the environment. As Speth (1992) has argued, the prospect of a transition to greatly increased sustainability may be viewed as both a technological and moral challenge. For developed countries, this could mean radical changes in the tension between environmental responsibility and commercial competitiveness. For less developed countries, it could greatly ease the tension between environmental responsibility and economic development.

This opportunity arises out of a coincidence between recent advances and future prospects in applied bioscience, and the possible emergence of a public mood favouring the application of a style of technology that is more compatible with the natural world than the technologies of the past. Over the years, there have been many occasions when the "push" of technical innovation has not matched the "pull" of society's needs. The advent of clean technology may mark the first occasion when the two forces are in harmony.

Yet, however strong this case may be, the shift in outlook will not be achieved without vigorous measures to inform people about the true nature of biotechnology and to motivate opinion leaders and other key players. There is a particularly keen need for greater mutual understanding and co-operation between business leaders and environmentalists. If the transition to a new generation of environmentally benign technologies is to be achieved, they will have to agree upon a common agenda.

Speth (1992) defines that agenda as one which "sees technology as part of the solution and not just part of the problem". It is a broad and heterogeneous agenda, ranging from the need to replace existing machinery and equipment with ecologically more acceptable versions, to the need for business leaders to reject adversarial attitudes in favour of new, co-operative and sustainable approaches to industrial production.

PROMOTING PUBLIC UNDERSTANDING

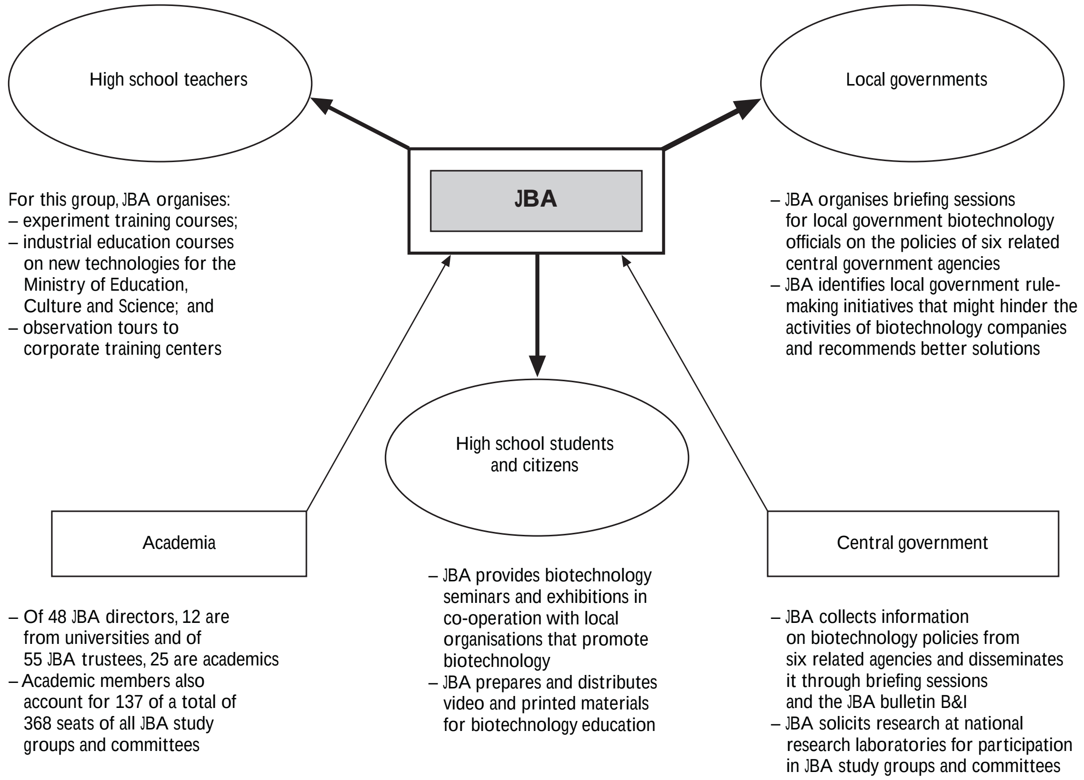
Experience from fields as disparate as formal education, advertising and political campaigning suggests that there is no universally appropriate strategy for promoting wider comprehension of a topic such as biotechnology. Efforts will need to reflect the nature of the societies in which those initiatives are to be taken. Overall, evidence from OECD countries indicates that while public *interest* in science and technology is high, public *knowledge* lags significantly behind (OECD 1996; Normile, 1996).

There are, moreover, wide disparities among countries in both areas. Even within continental Europe, approaches likely to be effective in France or Italy, for example, may not be appropriate in the different circumstances of Austria, Germany, or Switzerland. Nevertheless, in all countries, such initiatives will have to seek to help citizens understand evolving biotechnologies and their implications and to encourage citizens to influence the application of these technologies, if they wish to do so, through their political rights and in other ways.

One specific issue that needs to be addressed is that of the many positive roles that microbes play in the natural world other than as agents of animal and plant diseases. As Atlas (1996) has observed, the common perception of micro-organisms is as agents of disease, while the far greater populations of beneficial microbes, which are in fact essential to life on Earth as we know it, are neglected.

There is considerable scope for initiatives to promote wider awareness of the diversity of microbial activity. Projects which already do so are the Microcosmos Science Education Museum at Boston University and the American Society for Microbiology's Microbial Literacy Collaborative, based in Washington, DC, in the United States, and, in Japan, the Japan Bioindustry Association has also undertaken such projects (Figure 5.1). In addition to long-established channels for communicating with the

◆ Figure 5.1. ***Specific JBA activities to improve public acceptance of biotechnologies***



For this group, JBA organises:
- experiment training courses;
- industrial education courses on new technologies for the Ministry of Education, Culture and Science; and
- observation tours to corporate training centers

- JBA organises briefing sessions for local government biotechnology officials on the policies of six related central government agencies
- JBA identifies local government rule-making initiatives that might hinder the activities of biotechnology companies and recommends better solutions

- JBA provides biotechnology seminars and exhibitions in co-operation with local organisations that promote biotechnology
- JBA prepares and distributes video and printed materials for biotechnology education

- Of 48 JBA directors, 12 are from universities and of 55 JBA trustees, 25 are academics
- Academic members also account for 137 of a total of 368 seats of all JBA study groups and committees

- JBA collects information on biotechnology policies from six related agencies and disseminates it through briefing sessions and the JBA bulletin B&I
- JBA solicits research at national research laboratories for participation in JBA study groups and committees

Source: JBA.

public, travelling exhibits and science fairs and weeks (which have burgeoned in recent years) (OECD, 1997*a*) might be used to foster greater awareness of the positive activities of micro-organisms.

Atlas (1996) considers that changing the present, largely negative view of microbes through educational programmes that increase scientific literacy is crucial to public acceptance of bioremediation, for example. However, wider recognition of the vast amount of microbial activity beneficial to the environment and human society is also likely to encourage support for the harnessing of microbes, and biological agents generally, in other fields, such as clean industrial technologies.

While evidence cited earlier indicates a more favourable public stance towards biotechnology in many countries than might be apparent from the media and activities of campaigning groups, it is wrong to expect that greater public understanding of a technology will always lead to greater public acceptance of that technology. The reverse may even be true.

GROWING INTEREST IN CONSERVATION

A particular feature of the contemporary world is likely to be favourable to the public's endorsement of "clean" technology: the growing interest in many countries around the world in conservation and protection of the natural environment. As Lynch and Hutchinson (1992) have pointed out, the incorporation of environmental themes into education at all levels in the United States has accompanied, and in part inspired, this revolution in public attitudes.

Elementary school curricula, for example, now incorporate topics such as recycling and renewable energy. At the secondary school level, study of these topics is deepened and extended to include the concepts of global stewardship and environmental citizenship. Likewise, environmental studies are quickly becoming a part of liberal and scientific university curricula, while the basic disciplines of biology, physics, chemistry, engineering sciences, and Earth sciences are being illuminated by reference to environmental issues.

Clearly, initiatives of this sort are far from universal. There is an urgent need to strengthen and extend them, as well as for countries at differing levels of economic development to incorporate these messages in their school and higher education curricula.

Lynch and Hutchinson (1992) argue that the central issue of ecology – "how to sustain a rapidly growing and (necessarily) industrialising global population without provoking a Malthusian climax" – can provide a focus for these educational initiatives. The focus needs to be sufficiently clear and authoritative to express the environmental challenge as arguably the greatest single challenge of our time and to engage the hearts and minds of students.

But this is a message that may also appeal to a wider audience, to society as a whole. It could provide a favourable climate for the adoption of technologies which, as illustrated elsewhere in this report, have two distinctive features. They have characteristics which make them intrinsically "cleaner" than the alternatives, and offer greater opportunities for processes to be designed and operated in an ecologically acceptable fashion.

Making these advantages more widely known requires sound and sensitively planned initiatives in the realm of public information. Though the strategy needs to be determined country by country, in order to reflect cultural, educational and other differences, these are tasks for the immediate future if we are to reap the benefits of biotechnology applied to clean industrial products and processes.

REACHING DIFFERENT CONSTITUENCIES

As regards target audiences, pre-eminent among these are opinion leaders (including editors of major newspapers, magazines, and radio and television programmes); pupils and their teachers in primary and secondary schools; students following science, technology and other courses in the higher education sector; non-technical staff in the biotechnology and other industries; and local, national and supranational (*e.g.* European) politicians. The precise materials to be used in each sector need to be determined on the basis of both convenience and fashion. For example, videos and CD-ROMs are increasingly popular in schools, while many politicians prefer concisely written briefing documents.

The argument for targeting editors in the print media and broadcasting for their influence as formers of opinion is not a straightforward one. Newspapers, broadcasting channels and other media certainly have a continually renewed appetite for ideas, novelty, and material they believe will interest their audience. However, they can also have negative views of the causes for which their active support is solicited. There is a subtle distinction between attracting sustained media coverage of a topic of public interest and expecting journalists to campaign on its behalf. Efforts to involve the media in this latter sense are unrealistic and can be frustrating and/or counter-productive.

Nevertheless, there are strong grounds for placing information and ideas before editors. As gate-keepers, those in the print media have a far greater role than most individual journalists in deciding what topics their publications and programmes should cover, at what length, and in what style. Above all, they set the agendas that determine the themes that will be covered regularly, not only in news columns but also in longer feature articles and in influential pages such as editorials. Similar considerations apply to broadcasting.

Not least because of the keen interest of young people in the environment, schools are another important sector. As the OECD (1995) has suggested, a fundamental theme of educational approaches might be the life cycle of products with which students are familiar (see also Chapter 4 on life cycle assessment). For elementary school pupils, for example, a leather shoe could be the basis for discussions of cattle raising, the tanning trade, footwear design and assembly, distribution and disposal. Cleaner technologies could be contrasted with conventional ones at each stage.

Schools are highly appropriate communities within which to develop such ideas. A survey carried out by the University of Klagenfurt showed that middle and northern European schools are increasingly being "ecologised". In Austria, between 1992 and 1994, all 12 schools in the Weiz community underwent reviews to monitor their environmental performance. These highlighted weaknesses, such as the absence of heat control in classrooms (which lacked thermostats and insulation), and strengths, such as the use of recycled paper, waste separation, the elimination of aluminium and plastic containers, and the cultivation of indigenous plants in school grounds (OECD, 1997*b*).

As regards biotechnology *per se,* efforts to introduce the subject into classrooms in the San Francisco Bay area (California) have been highly successful. However, such initiatives may soon falter, if, for example, key teachers move elsewhere or materials obtained through an initial grant run out. Mascarenhas (1997) points out the pressing need to sustain such activities over the long term.

The classroom is a setting in which long-standing attitudes and opinions can be formed, especially when they are endorsed by a respected teacher. In several countries, this lesson has been learned over the past decade as a consequence of school visits by animal rights lobbyists. While such visits may be legitimate, they can make pupils highly resistant to subsequent arguments as to why some humane animal experimentation is necessary in the present state of medical knowledge.

HIGHER EDUCATION AND POLITICS

In the higher education sector, the principal need is to broaden the training of biotechnologists and other specialists. Concepts such as life cycle analysis and environmental sustainability need to be thoroughly integrated into their education and thus their future thinking.

As Troxell (1992) observes, "We will need people who have a comprehensive understanding of diverse technologies, the ability to determine the entire system of an industrial process, and the ability to determine the pluses and minuses of each component of an industrial process for total optimisation." In the past, students' training has often failed to give them sufficient breadth of knowledge to make them familiar with all aspects of an industrial process. In many cases, for example, a chemical engineer engaged in developing a process has not had to consider the environmental impact of obtaining raw materials, nor even, in some instances, ways of disposing of by-products. These aspects of the operation have typically been the concern of other specialists.

Similar shifts in perspective are required in the education of non-scientific personnel who will work in industry, and in re-education of existing staff, through in-service courses, for example. For example, some of the changes to be encouraged in the habits of thought among staff charged with financial responsibility may appear to work against what had previously been their professional responsibilities. Moreover, as the OECD (1995) has pointed out, rational managers are unlikely to select cleaner technologies and products unless they improve the competitive position of their companies, and unless governmental initiatives help to create demand for them.

Ehrenfeld (1994) calls for ‘‘industrial ecology’’, embracing clean technology, Life Cycle Assessment, and environmentally conscious manufacturing, to be incorporated into university teaching not only of science and technology but of other subjects as well. He observes that educators are just beginning to recognise the need to educate professionals in fields such as business administration, where the environment has been virtually ignored in the past.

Professionals of this sort will have to spend much of their time coping with the requirements of existing regulatory authorities. Nevertheless, it is important to instil an awareness of the broader context of industrial sustainability in students during their training, so that they can anticipate and avoid problems, rather than allow problems to develop and require solution later. Ehrenfeld argues that the technological consequences of societal activities should become a more explicit part of the education of professionals heading for planning, policy, managerial, and design careers.

Helping to educate the next generation of environmental scientists and engineers is an objective of a scheme launched by the US National Science Foundation and the Lucent Technologies Foundation in 1997. Researchers across the country have received grants intended to advance industrial ecology and to encourage businesses to integrate pollution prevention into their day-to-day operations. Each of 18 grants will support an individual or team involved in research or teaching to help industry design processes that prevent pollution and create environmentally friendly products.

At least one company has already made considerable efforts to assess its own activities from a wide environmental perspective and taken a range of initiatives accordingly, the Danish company, Novo Nordisk, based in Bagsvaerd, Denmark. A description is given in Box 5.2.

Since even the design and evaluation of more ecologically desirable industrial processes take time, such processes are likely to be adopted over a substantial number of years. While this trend can be accelerated (or slowed) as a result of public and political pressure, it may extend beyond the time

Box 5.2. **One company’s approach to environmental reporting**

In 1974, when Denmark’s first Environmental Protection Act came into effect, Novo Nordisk, a manufacturer of insulin and enzymes, created an independent environment department, to ensure that it conformed with official protocols. In the late 1980s, however, the company increasingly recognised a need to maintain a dialogue with customers, neighbours, environmental organisations, students, investors, employees and other groups.

In the run-up to the 1992 Rio Summit (see also Chapter 6), the International Chamber of Commerce (ICC) drew up a 16-point Business Charter for Sustainable Development, and allowed companies to declare their willingness to register, control, and report on their environmental performance to the public. Novo Nordisk signed the charter, and uses it as a guide for its environmental work and policy. The company has undertaken to communicate openly, both internally and externally, and publishes an annual *Environmental Report* so that interested parties can follow the company’s progress in environmental matters. Recent reports have presented detailed pictures of the consumption of resources and the environmental impact of all Novo Nordisk’s production plants world-wide and also the company’s compliance with legislation around the world.

The *Environmental Report* is important internally and also serves as a source of information for those outside the company. It motivates staff by highlighting environmental goals and the results of the efforts made, and helps identify new problem areas, thus serving as a catalyst for improvements in Novo Nordisk’s environmental work. The company believes in face-to-face dialogue in discussing environmental issues, especially in complex areas such as biotechnology. Large numbers of schoolchildren and students visit the company, and its environmental staff appear regularly at conferences and on external courses.

horizons within which politicians tend to work. Nonetheless, long-term issues such as global warming and the preservation of genetic diversity have appeared on the political agenda in recent years and have received serious national and international attention.

These developments thus contradict the common criticism that politicians are concerned only with their own, possibly very short, political lifetimes. They also suggest that politicians are likely to be receptive to briefing materials on clean technologies – a topic that brings together global environmental and resource concerns and financial and business issues – especially when these matters are raised by their electorates. There is a clear need to enhance the scientific awareness of government regulators and their constituencies on the issue of biotechnology for clean industrial products and processes.

THE TIME FACTOR

Efforts to promote greater public understanding of biotechnology must take account of the differing state of public opinion and how it is formed in different countries. A recent review (*Nature*, 1997) has highlighted contrasts between the United States, Russia, Japan, Germany, France and the United Kingdom in public concern over emerging technologies and in the development of bioethics as a discipline. However, as the 1996 Eurobarometer findings have suggested, there may, in general, be increasing interest in the moral justification (or lack thereof) for certain avenues of research and development.

Initiatives concerned with perceptions of biotechnology also need to be founded upon a recognition of the dynamic rather than the static nature of public opinion. In addition to the 1996 Eurobarometer data cited above, three recent developments illustrate this vividly. First, an opinion poll conducted in 1996 in Allensbach, Germany, showed that only 29 per cent of 1 000 individuals thought that the risks of genetic engineering were so high that it should be banned (Abbott, 1997). This compared with 40 per cent in a similar poll carried out eight years previously.

Second, a public opinion survey conducted in Austria in 1994 (Torgersen and Seifert, 1997) indicated that while the level of support for genetic engineering was lower than in other parts of Europe, the perception of risk was also comparatively low. The key factor seemed to be a conservative attitude towards new technology in general, rather than any concrete views about its possible dangers. However, when the first releases of recombinant organisms were planned in Austria in 1996, there was widespread rejection and increasing anxiety about associated risks.

Third, an experienced commentator on science in Japan has pointed out (Swinbanks, 1997) that while scientists "are generally held in high regard in Japan, and their views tend to be accepted uncritically by the public ... that faith has been severely strained by the events of the past year". Particularly influential was a scandal over contamination of blood and blood products by HIV, and an incident in which thousands of schoolchildren suffered from severe food poisoning caused by the pathogenic strain O157 of *Escherichia coli.*

Events in the United Kingdom during 1996 – including an *E. coli* O157 epidemic and the appearance of cases of Creutzfeldt-Jacob disease in humans which are said to be associated with bovine spongiform encephalopathy in cattle – underlined the way in which specific concerns can lead to more general unease about science and scientists. They may, as in this case, also awaken or reinforce anxieties about biotechnology, despite the fact that neither incident actually involved biotechnology. Whether such anxieties deepen or are stilled depends not only upon the material facts but also upon the nature of measures to promote public understanding and of responsive measures to explain what has happened when adverse developments do occur.

Opinion surveys such as those cited above show that many members of the public in many countries are still making up their minds about biotechnology and genetic engineering. Answers to questionnaires invariably include substantial numbers of "don't knows". The opportunities to influence public opinion, for good or ill, are clear. Moreover, for the reasons given above, the mood of the public, and its younger members in particular, is likely to be receptive to the idea of applying biotechnology to the "greening" of industry, the safeguarding of the environment, and more prudent planetary housekeeping.

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NATIONAL AND INTERNATIONAL POLICIES*

- **International agreements often serve as a basis for national policies and legislation on clean industrial products and processes.**
- **Government policy is a major driving force for clean technologies but can have positive or negative effects, so that both of these require careful consideration.**
- **While many countries consider biotechnology as a critical enabling technology, they have not identified it as a preferred tool for achieving cleaner products and processes.**
- **Policies that affect the marketplace can be most effective in driving change.**

INTRODUCTION

Government policy, as reflected in regulation, legislation and guidance is recognised as a major driving force behind cleaner technologies, and in many cases and countries, the single most decisive factor in their development and diffusion. This chapter therefore undertakes an initial analysis of certain areas of policy and legislation, which were chosen because they can drive cleaner industrial products and processes and might cover sectors or activities where biotechnology may be beneficially applied. Its goal is to illustrate how government action can trigger or facilitate the move towards cleaner industrial products and processes. Unlike other chapters of this report, which are quite broad-based and comprehensive in their coverage, as in the case of industrial sectors likely to be penetrated by cleaner biotechnological process technologies (Chapter 2) or R&D priorities and the related scientific and technological bottlenecks (Chapter 3), this chapter presents only a sample of national policy and legislation.

The three countries examined – Canada, Germany and Japan – are, like many other OECD countries, concerned with and committed to cleaner industrial products and processes. They offered their co-operation in this area as part of their active support for this report. The information is based on interviews with policy makers and experts in the respective countries and on the relevant literature. Annex 6 contains selective summaries of their laws and policy initiatives. While it would certainly have been valuable to include comparable information on other countries, a comprehensive review of the OECD's 29 Member countries and a few important developing countries was deemed impracticable at this juncture.

It should be borne in mind that these three countries, on three different continents, share many features: all are relatively large, highly industrialised, and have a high level of environmental awareness as well as a strong science and technology base. At the same time, differences in their legal systems and practices may affect the move towards cleaner products and processes. The similarities raise questions that must, for the moment, remain unanswered. Would coverage of many other countries – small but highly industrialised, poorer, or with very different legal and social traditions – yield radically different conclusions about the relevance of government policy and legislation? Some of the common elements and conclusions pertaining to the three countries are likely to be valid for many others as well, although further investigation would be needed to ascertain this.

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* This chapter was drafted under the responsibility of Mr. V. Aidun, Industry Canada, replacing Mr. D. Mahon (Canada).

THE INTERNATIONAL DIMENSION

One of the most visible marks of policies for cleaner technology is their strong international dimension, with roots in international agreements and conventions. This international dimension can explain many similarities in national policies. The 1992 Rio de Janeiro Conference on Environment and Development (UNCED), and particularly its Agenda 21, has played a key role in this. The international and national implications of the conference are summarised in Box 6.1.

Box 6.1. **The Rio Declaration: international and national implications**

In 1992, Rio de Janeiro hosted the United Nations Conference on Environment and Development (UNCED), following the recommendation of the Bruntland Commission (Bruntland, 1987). The UNCED report established Agenda 21 as the action plan for governments and international organisations and the Commission on Sustainable Development (CSD) as the UN body responsible for co-ordinating international action to achieve the objectives of Agenda 21.

UNCED established a policy framework, and governments agreed to a set of principles or policies that would allow the world to move to a regimen of sustainable development. These policies are based on concerns for the environment on which life depends and on the need for economic growth and wealth creation. The policies support the premise that industry must be based on sustainable use of all of the Earth's resources, including resources not commonly associated with industrial development, such as air, water, and natural habitats. Implicit in the concept of sustainability are approaches that protect the environment and reduce the negative environmental impacts of both use and development. In an industrial context, this concept has been embodied in the term ''clean industrial products and processes''.

Because it was recognised that most issues and policies could best be addressed at national level, it was decided that countries should report annually on their efforts to implement the policies to the CSD, which in turn is responsible for reporting the results to the United Nations. In particular, countries report regularly on legislative, regulatory, industrial and social activities pertaining to biotechnology, the area covered by Chapter 16 of Agenda 21. Chapter 16 aims to foster the development of international principles to ensure the environmentally sound management of biotechnology, engender public trust and confidence, promote the development of sustainable applications of biotechnology, and to establish appropriate enabling mechanisms, especially in developing countries, through the following activities:

- increasing the availability of food, feed, and renewable raw materials;
- improving human health;
- enhancing protection of the environment;
- enhancing safety and developing international mechanisms for co-operation;
- establishing enabling mechanisms for the development and the environmentally sound application of biotechnology.

At the same time, UNCED recognised that certain issues were global in character and could only be effectively addressed through co-ordinated international action. Therefore, UNCED established several bodies, mainly under the administrative umbrella of the United Nations Environment Program (UNEP). These conventions include the Convention on Biological Diversity (CBD), the Convention on International Trade in Endangered Species (CITES), and the Convention on Climate Change; these complement conventions already in existence, such as the Basle Convention on Hazardous Waste, the Vienna Convention on Protection of the Stratosphere, and the Montreal Protocol on Ozone Depleting Substances. Such conventions address specific concerns, but they also give the countries that ratify the convention the authority to develop appropriate protocols, or international legislation, that signatory countries are bound to enforce if the protocol or legislation is ratified. This is the case for the Montreal Protocol and the CBD's current activity to develop a Protocol on Biosafety for transboundary movement of living modified organisms.

There is, therefore, a hierarchy of international action that drives the movement towards cleaner industrial products and processes. Policy established under UNCED is primarily national in character but is reviewed and analysed by the Commission on Sustainable Development. International policy on specific issues is dealt with under conventions and may result in international regulation through protocols developed under the conventions. These protocols are then translated into national legislation for action.

However, not all national policies in this area have their origin in international developments. Some countries indicate that they have had national legislation in favour of cleaner technology for many years and predate some of the decisive international conventions. There is continuous interaction between national and international policy developments in this field, and the balance between the two varies over time and according to the country.

Nonetheless, following the Rio Conference, there has been increasing awareness that to ensure sustainable development as well as economic growth, industrial processes require fundamental changes. The need to reduce the production and release of pollutants concerns national economies, the quality of a country's and the world's environment, and the fact that the notion of a "disposable society" cannot be sustained. Governments, international policy bodies such as the United Nations and the OECD, and industry itself have therefore undertaken initiatives to promote concepts for improving industrial processes to reduce the quantity, and in many cases the type, of by-products and contaminants and to develop new products and processes that reduce the negative impacts of industrial processes on the environment.

Industrial activity can negatively affect many aspects of the environment, including air quality, water quality, soil productivity, and even the productivity of the oceans and the world's climate. While no single action can, in and of itself, effect a move towards cleaner industrial practices, the combined impact of many direct and indirect actions at both international and national level has led to significant changes in industrial activity.

There is a developing understanding that locally, regionally and globally there needs to be improvement in resource use and a reduction of the amount of waste and pollutants generated by industrial activity. It is based on a realisation of the limitations on natural resources, including renewable resources, and a drive to improve industrial efficiency as a means to protect the environment and human health on national, regional and global scale. Pollutants generated and released in one country may move to others through air, water or as the waste generated in finished products. The cost to society in remediating polluted media is increasing each year.

Box 6.2. **Global warming**

The third session of the Conference of the Parties to the United Nations Framework Convention on Climate change (COP3), held in Kyoto, Japan, on 1-10 December 1997, agreed on a protocol which includes each party's quantitative commitment to reduce its emissions of greenhouse gases, such as carbon dioxide (CO_2) by 2010. The protocol specifies that the European Union will commit itself to reducing its greenhouse gas emissions by 8 per cent by 2010 from the level of 1990 (base year), the United States by 7 per cent, and Japan and Canada by 6 per cent.

As an essential element in achieving this goal, industry must reduce energy consumption in order to maintain development while helping to meet these targets. This would include a shift from present petrochemical industry processes, which consume large quantities of energy under conditions of high temperature and pressure, to more energy-efficient biological processes, which use renewable resources such as biomass to produce useful substances under normal temperatures and pressures. For example, future processes will focus more on producing efficiently alternative fuels such as ethanol, which contribute less to global warming and are also likely to produce environmentally benign products, such as biodegradable plastics, which break down in natural settings after use.

As a result, biotechnology should become an increasingly valuable tool for developing environmentally friendly products and processes and for preventing the Earth from warming.

COMMON ELEMENTS IN NATIONAL POLICIES

Recognising the need for cleaner industrial practices, many governments have developed policies and legislation to reduce the use or generation of chemicals or processes that could degrade the environment or increase risks to human life and health and to animals.

In fact, the number of policy and legal initiatives that encourage cleaner technology, and are therefore implicitly relevant to clean process biotechnology, is large and increasing. Countries can already identify policies which have had positive effects, not only on the environment and sustainability, but also on technological progress and economic development. In some countries, environmental protection laws are leading to new, innovative products and processes which increase industrial efficiency and to the promotion of a thriving industrial sector. As a result, new jobs have been created, and it is expected that many more will be created in coming years. However, other regulatory policies have been seen as inhibiting scientific, technological or economic development, and even environmental protection by the best available means, and have been identified as requiring modification. Because the legal and regulatory framework for cleaner industrial products and processes can have negative as well as positive effects, both of these need to be considered.

For the moment, a study of Canada, Germany and Japan suggests some common elements. First, there is no international or national legislation that explicitly identifies biotechnology as a preferred tool for achieving cleaner products or processes. With respect to opportunities for using biotechnology to achieve cleaner products and processes, countries have identified biotechnology as a critical ''enabling technology'', a category that must be placed in a context relevant to achieving cleaner industrial products and processes.

Because they are pervasive, enabling technologies are not usually the object of specific legislation. Generally, policies tend to articulate objectives, but do not identify in detail the means to achieve the desired ends. Therefore, when policy has been developed for one sector or another, specific technologies are rarely mentioned. In very broad policy areas, such as reduction of waste or energy use, changes in consumer lifestyles, or recycling, various technological options may be available.

Moreover, each country implements policies in a manner that is appropriate to its national culture, with mixes of policy, legislation, voluntary initiatives, and economic tools. Certain elements are relatively new and are becoming more common in the drive to sustainable development. One is the move both to involve and to direct society, as the final consumer and therefore a potential prime mover, which is particularly visible in Japan.

Because much of the drive for cleaner industrial products and processes is linked to concern about environmental pollution and waste generation, most legislation and policies are directed towards prevention of pollution and waste. Their implementation, for instance to reduce energy use or energy waste in manufacturing, results in further legislative or regulatory requirements. As specific sectors or processes are identified in legislation, and as targets are set either by policy or by voluntary initiatives, the need for innovation increases.

Policies which involve the general public potentially have the most far-reaching effects. If consumers' lifestyles change and demand for cleaner products becomes the norm as clean products are identified, then manufacturers must adapt to meet this demand. Policy then follows the wishes of the public and becomes an economic instrument which drives changes in manufacturing procedures.

Certain sectors have been clearly identified as areas for cleaner practices. Each of the countries studied has identified the need to reduce energy use for economic reasons by moving to more energy-efficient processes. Countries have also sought changes in energy production processes through innovative energy generation systems, since the combustion of fossil fuels is an element in the production of greenhouse gases and a component of global warming.

Waste generation and disposal is another area that has received significant attention. The focus has been on reduction of waste generation through both voluntary and regulatory initiatives. This is evident in initiatives to increase the use of recyclable materials in product development and in the increased use of renewable materials in products. Industry has addressed this issue in several ways, very often through Life Cycle Assessment (see Chapter 4).

Moreover, specific toxic materials are identified and targeted for reduction or elimination. The objective is to change the industrial processes that rely on these chemicals. The alternatives can then be specified. Both internationally and nationally, specific chemicals have been identified for reduction or elimination. In general, these are persistent, bioaccumulative, and toxic; in particular, the highly chlorinated chemicals have been targeted for reduction or elimination. For example, the OECD has initiated action to control the industrial use of toxic chemicals through the New Substance Notification Scheme, which requires notification and assessment of new chemicals prior to market introduction. Complementary national policies and legislation respond to international requirements and establish a national basis for action regarding the production and release of toxic substances. These initiatives have also been complemented by actions taken voluntarily by industry.

The purpose of moving towards cleaner industrial products and processes is to achieve specific societal, economic and safety objectives. Two aspects of the legislative and policy arena which are not addressed in this chapter are research policy, dealt with in Chapter 3, and economic policy regarding cleaner products and processes, which was discussed in *Technologies for Cleaner Production and Products* (OECD, 1995).

Areas that would benefit from further study include:

- sectoral changes, research trends and specific research projects in industrial biotechnology, to determine if that research parallels the policy and legislative objectives;
- legislation and its effects on biotechnology for cleaner industrial products and processes;
- the interaction between research and legislation as drivers;
- the relationship between economics and legislation.

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CONCLUSIONS AND POLICY IMPLICATIONS

This report reviews biotechnology as a means to achieving cleaner industrial production. It sets biotechnology in a national and broad global context, and highlights the industrial perspective for achieving sustainability. The crucial feature of the clean technology paradigm is that it shifts attention and actions from remediation to prevention of environmental degradation. The evidence shows that biotechnology can contribute greatly to the ''greening'' of industry, and is economically competitive.

It is paradoxical, therefore, that biotechnology's penetration into certain sectors of industry has been slow. Many of the explanations advanced in the past are no longer valid. Among the more outdated are the notion that the cleanliness of biotechnology has not been proven, that the costs and risks are too high, or that the scale of operations is too restrictive. Examples given in this report show, instead, that arguments for deferring the adoption of biotechnology based on limited operating scale or throughput, or because of a perceived need for major re-equipping of manufacturing plants, are no longer tenable.

The transition to cleaner industrial manufacturing does not necessarily require a change to completely new and costly plant and equipment. Often, the introduction of biotechnology unit stages will achieve the desired result, or existing plant can be modified for biotechnological processes. However, a bridge is required from basic research to final implementation, and it can best be provided by partnerships between government, academia and industry which demonstrate applicability. In addition, improved cleanliness must be demonstrated by rigorous analysis.

The following ten points summarise some of the central findings of the report and indicate what has to be done by the main stakeholders – mainly government, but also industry, the public and the scientific community – to reach a highly desirable and achievable goal. Because joint action is seen as crucial, discussions among these stakeholders is essential. Only such interaction can define the agenda and the appropriate roles of the interested parties in implementing these recommendations.

Global environmental concerns will drive increased emphasis on clean industrial products and processes. Biotechnology can contribute to reduced energy consumption and lowered production of pollutants such as greenhouse gases and acid rain. These contributions will be more significant in some industrial sectors than in others. The use of biorenewable feedstocks to replace fossil fuels can result in carbon-dioxide-neutral processes that will further lower atmospheric build-up of carbon dioxide. Biotechnology can produce cleaner fuels that will also help alleviate other atmospheric pollution problems.

Biotechnology is a powerful enabling technology for achieving clean industrial products and processes which can provide a basis for industrial sustainability. In addition to chemical and physical engineering approaches, biotechnology is becoming increasingly competitive in achieving reduced energy and material consumption and minimisation of waste and emissions. Biotechnology has the advantage of building upon biological systems that have evolved over many millions of years and are continuously self-improving, and it is widely applicable. Biotechnological processes, especially enzyme-based technologies (biocatalytic processes) tend to operate at lower temperatures and to produce fewer and less toxic waste by-products and emissions than conventional chemical processes. Industries should use biotechnology where it can provide clear environmental benefits.

Measuring the cleanliness of an industrial product or process is essential but complex; Life Cycle Assessment (LCA) is the best tool currently available for making this determination. It is necessary to examine processes in their entirety (''from the cradle to the grave'') to determine energy and material balances and hence their cleanliness. For informed industrial decision making, it is indispensable to know what is "clean" or "cleaner". LCA, or a similar analysis, is best performed at an early stage of an R&D project, when it can help determine the environmental benefits to be obtained from a clean biotechnological process. There is a need to harmonise LCA with other methodologies, including "green accounting" and other types of goal setting. Simple decision-making rules are needed to establish the *boundaries* of an LCA (where the process that is being analysed begins, and where it ends) and the *weighting* (relative importance) of the factors included in the analysis. Improvement of LCA procedures and the development of additional tools for assessing cleanliness and relating environmental and economic benefits will enhance the industrial utilisation of clean technologies.

The main drivers for industrial biotechnological processes are economics (market forces), government policy, and science and technology. These drivers for biotechnology for clean industrial products and processes vary among industrial sectors. Market forces respond to the profitability of incorporating clean technologies; government policies reflect public interest in a cleaner environment; science and technology forms the foundation and provides methodologies for establishing technical feasibility. These three factors act in concert – none, on its own, will drive the use of biotechnology.

Achieving greater penetration of biotechnology for clean environmental purposes will require joint R&D efforts by government and industry. The private sector will rarely make the investments necessary for developing and incorporating biotechnological processes into existing systems unless the benefits to be obtained are proven. This is especially true for a new technology when profit margins are uncertain and not readily quantifiable relative to conventional technologies. Biotechnology has proven its worth for high-value speciality chemical production, and a number of cases have demonstrated its competitiveness for the production of commodity chemicals. Governments need to assist in the demonstration, development and dissemination of relevant information, and to encourage public awareness and capacity building. There is a need for partnerships that integrate the roles of government, industry and the public to achieve industrial sustainability and utilisation of biotechnology.

For biotechnology to reach its full potential as a basis for clean industrial products and processes, beyond its current applications, additional R&D efforts will be needed. New biocatalysts and bioreactors will be required to gain penetration into industries that traditionally have employed petrochemical feedstocks and high temperature/high pressure reaction conditions. Exploration of biodiversity, including in extreme environments, will be useful for finding new sources of biocatalysts. Combinations of biocatalytic activities, through the use of bioconsortia and recombinant DNA technology, will be needed to meet many industrial process requirements. Long-term stability of biocatalyst activity and minimisation of water requirements through the design of special bioreactors, immobilised cells and enzymes, and non-aqueous biocatalysis, will be crucial for achieving greater cleanliness and reducing costs. Integrating bioprocessing into existing commercial operations requires additional engineering developments. Government and industrial support for R&D efforts, including the facilitation of voluntary co-operative agreements, will be important for innovation and is an essential underpinning for the advancement of biotechnology. Such joint efforts on demonstration projects are needed to bring basic research to full industrial implementation. In addition, academia is called upon to provide fundamental research and training in support of biotechnological applications.

Because biotechnology, including recombinant DNA technology and its applications, has become increasingly important as a tool for creating value-added products and for developing biocatalysts, there is a strong need for harmonised and responsive regulations and guidelines. Regulations governing biotechnology must be dynamic and responsive enough to account for the fact that science and technology are constantly evolving, as is the knowledge and familiarity of scientists and regulators. International harmonisation of the principles underlying government oversight, particularly with reference to industrial uses of recombinant biocatalysts, is central to removing obstacles to the wider industrial penetration of clean biotechnological processes. Government policy should streamline relevant guidelines and oversight systems in this context to ensure that they are clear and scientifically based, so that clean industrial products and processes based on modern biotechnology can be achieved. Clarification of the use of good industrial large-scale practices, particularly regarding the boundaries of contained use, and concise guidance for risk analysis will be of great assistance to industries considering biotechnology for clean industrial processes.

Market forces can provide very powerful incentives for achieving environmental cleanliness objectives. Markets generally are the most important initiators of technological diffusion. Although the public will support government policies that encourage clean industrial processes and products, customers are reluctant to pay for any costs added by clean production processes. Market mechanisms allow for great flexibility in designing responses to publicly determined environmental aims; industries can react to pollution control in various ways, including process change, technology development, and product modification. Economics, including capital investment and the cost of complying with environmental regulations, underpin industrial decisions on implementation of new technology. Market pressures tend to result in rapid industry response, especially when they have significant impact on profitability. Market pull is in fact an effective means of gaining industrial penetration for clean biotechnological processes and the production of ''green products''. Market forces, with their ability to provide very powerful incentives for achieving environmental objectives, are valid alternatives to regulation.

Government policies to enhance cleanliness of industrial products and processes can be the single most decisive factor in the development and industrial use of clean biotechnological processes. Legislation, regulation, government guidelines, standards, government procurement and government supported R&D can encourage or discourage – accelerate or delay – the use of clean processes based on biotechnology. Obstacles can arise from the following: absence of policy or enforcement, insufficient international harmonisation, policy uncertainties and contradictions, and policies that ignore the particular conditions of individual sectors. Government policy should promote the best clean technological processes and encourage their wide dissemination for industrial use. Governments can provide incentives for employing clean technological processes so that biotechnology can be used when it is found to be appropriate on the basis of economic analysis and assessment of environmental cleanliness.

Communication and education will be necessary to gain penetration of biotechnology for clean products and processes into various industrial sectors. Public support for clean industrial products and processes is necessary for widespread industrial penetration of clean biotechnology. Risk assessment, conducted on a scientific basis, is essential for increasing transparency, and gaining wider acceptance of biotechnology. Responsibility for risk management and risk communication is handled in different ways in different Member countries. Greater understanding of biotechnology among the public, industrial managers and engineers, and government policy makers/regulators is crucial. Communication via the media is important to highlight the benefits and limitations of clean biotechnological processes. Easily accessible formal and outreach educational programmes are needed to inform the public about biotechnology and clean industrial practices.

Annex 1.1

MODELS OF INDUSTRIAL SUSTAINABILITY*

Traditionally, industrial processes have been structured as linear assemblies of unit stages, frequently operated as if they were independent and as a single throughflow of materials and energy. Such patterns assume unlimited resources and represent what is known as type I ecology. In contrast, type II ecology, which is based on interactive biological communities and limited resources, is quasi-cyclical and more efficient than type I ecosystems, but is not sustainable over long periods because flows are largely unidirectional. Sustainable biological ecosystems (type III), instead, are almost completely cyclical; resources and wastes are not defined or differentiated (Graedel, 1997) because the waste of one ecosystem component is the resource for another. Except with respect to input from photo- and chemi-synthetic sources, type III ecosystems are cyclical and hence sustainable.

Various models of industrial sustainability have been proposed. One is based on four nodes representing materials provision, materials processing/manufacture, consumption, and waste processing. The closer the operation of the nodes, the closer the overall system approaches cyclic flow, and the closer it approximates type III ecology. Graedel (1997) views current industrial sustainability as one in which the interests of three actors – raw materials supplier, manufacturer, and customer – are basically decoupled and relatively independent. Thus, approximating type III ecology will require closer co-operation among suppliers, equipment and process designers, and process engineers. Design for environment (see Chapter 3) offers a way to appraise the choice of raw materials, the minimisation and specification of air emissions and liquid and solid wastes, designing for energy efficiency and recycling during manufacture and after use. Graedel argues that if industrial sustainability is to be truly responsive to global health and environment concerns, those concerns must be ranked; he proposes the ‘‘somewhat arbitrary ranking’’ of 12 major environmental impacts. Annex Table 1.1 relates issues considered to be important in industrial design to their environmental impacts and thereby begins to prioritise actions that should lead to clean technology.

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* All references made in the text of these annexes can be found at the end of the relevant chapters.

Annex Table 1.1. **Relationships between design issues for clean technology and environmental impacts**

Design issues	Environmental impacts											
	1	2	3	4	5	6	7	8	9	10	11	12
Raw materials		L						M				
Air emissions	L		L	M			M		M	M	M	M
Liquid waste	M				M							
Solid waste	L					M						
Energy efficiency			M						L			
Recycling		L				L		L				
Land-use change*		M				M			M			

As defined below:
1 = the need to minimise or eliminate toxic effluents
2 = the need to protect biodiversity
3 = greenhouse warming
4 = destruction of the ozone layer
5 = quality of ground and surface waters
6 = exhaustion of appropriate landfill sites
7 = production of photochemical smog
8 = depletion of mineral deposits
9 = loss of atmospheric oxidising capacity
10 = production of acid rain
11 = corrosion in air and liquid environments
12 = deterioration of atmospheric visibility resulting from population or agriculture increase
M = major impact
L = lesser impact
* resulting from population or agriculture increase

Source: Graedel, 1997.

Annex 1.2

NOVEL CLEAN CHEMISTRY

CATALYSTS

Chemists have been very successful in developing novel catalysts which are making significant contributions to clean industrial processing:

- Phase transfer catalysts like crown ethers permit cleaner reactions over the whole range of separate phases (immiscible liquids, solid-liquid, liquid-gas).
- Certain catalysts, such as lanthanum triflates used for nitration reactions, prevent the generation of hazardous by-products.
- Chemical catalysts with chiral properties (chirality is a stereoproperty of some molecules that gives them left- or right-handed configuration). Chiral intermediates and products are particularly important because of their biological properties. In the marketing of pharmaceuticals and agrochemicals, production of pure stereospecific molecules is becoming *de rigueur*. Already, some countries are proposing an active ingredient tax that will force these and other industries to provide pure stereo products.

R&D on chiral chemical catalysts is at an exciting stage; opportunities that are appearing include:

- *Heterogeneous catalysts:* Alkaloid-rendered chirality of metal catalysts such as platinum, palladium, iridium and ruthenium. Example: chirally selective hydrogenation.
- *Lithium amide bases:* Specifying the chirality of the base enables either chiral version of the product to be synthesised. These catalysts are easily separated from reactants, thus facilitating re-use. Example: introduction of asymmetry into symmetric cyclic chemicals.
- *Polyaminoacids:* Homogeneous amino acid polymers can have catalytic properties and, because the catalysts themselves can be made in either chiral form, the chirality of the product can be specified. Polyleucine is a paste-like material, insoluble in organic media, and is readily recovered and re-used. Example: conversion of alkenes to epoxides.

REACTION MEDIA

Supercritical fluids have a number of industrial uses, for extraction, microprecipitation, separation, and as solvents and chemical reactants. The use of supercritical fluids promises to make chemical industries safer and cleaner, and it has been estimated that the size of some chemical manufacturing plants might be reduced by an order of magnitude as a result of their introduction. Example: supercritical CO_2 can be used for solubilising materials such as polymers, proteins, and metal oxides, thereby improving the environmental load from organic/halogenated solvent-intensive industries.

Ionic liquids are ionic solids which have been heated above their melting point (chloroaluminate III, for example, is liquid at room temperature). These materials have a very wide liquid temperature range and are being hailed as designer solvents and the basis of a new industrial technology.

SUPPORT MATERIALS

The chemicals industry has developed a large range of materials that function as catalysts and/or supports for reagents that also present waste minimisation opportunities. Among the attractive features of solids in this context are their selectivity, ease of recovery, and their replacement of stoichiometric by catalytic processes. Example: a new generation of nano-polymers, the so-called dendrons and dendrimers, are rapidly creating interest. These globular, tree-like structures may provide opportunities for clean industrial processing, given the diversity of design properties (catalytic, conducting, paramagnetic, photon absorbing) that can be built into their structures.

REACTION ENHANCERS

Both electrochemistry and sonochemistry (the effect of ultrasound) can bring about demonstrable waste minimisation in chemical syntheses. Sonochemistry, for example, can accelerate reaction rates, increase product yields, stimulate catalyst activation, and lead to the simplification of procedures (*e.g.* reactions made under conditions of ambient rather than very high pressure).

Annex 2.1

RECENT BIOTECHNOLOGICAL DEVELOPMENTS ADDRESSING THE NEEDS OF PROCESS CHEMISTRY

While biological catalysts possess many attributes that make them attractive for process chemistry, such as high turnover numbers and wonderful selectivity and specificity, they are not very stable as a class, and this poses a major problem for their industrial use. In nature, enzymes are replaced when they wear out in living cells, but in a chemical plant replacement is time-consuming and costly. Three sorts of solutions have recently been offered: stabilisation of naturally labile enzymes, development of naturally stable enzymes, and use of intact living systems to produce chemicals.

Altus Biologics, a subsidiary of Vertex, has commercialised cross-linked enzyme crystals (CLEC®). Many enzymes can be crystallised, so that enzyme molecules occupy repeating points in a regular three-dimensional array. If such an enzyme crystal is chemically cross-linked, so that the molecules are covalently attached to each other and cannot diffuse away, the individual enzyme molecules retain catalytic activity, and that activity is often hundreds of times more stable than the same enzyme in solution. The crystalline form of the catalyst is convenient to handle in the process environment. However, while CLECs address a major difficulty, there is still room for improvement. The crystallisation and cross-linking processes are not readily applied to all enzymes, and enzyme molecules in the centre of the crystal are kinetically hindered from access to small molecules and sterically hindered for large substrates. Nonetheless, the marketplace has received CLECs well, and the technology seems likely to widen the range of processes amenable to biocatalysis.

Although enzymes from animals, plants and many bacteria are often labile, there is nothing inherently labile about the underlying peptide structure. Indeed, companies such as the Diversa Corporation are busy discovering and developing enzymes from microbial biodiversity that are much more stable than conventional ones. They often start with enzymes from so-called extremophiles, organisms that grow under extreme conditions of pH, temperature or pressure, and they sometimes use a process called “directed evolution” (discussed in Chapter 3) to improve the properties of the starting material. Directed evolution is an iterative process of mutagenesis and selection that allows the experimenter progressively to change an enzyme’s properties towards those more desirable for process chemistry.

Most recently, a new company, Photosynthetic Harvest, Inc. (PHI), has devised a way of using living plants to produce continuously a wide range of chemicals. These chemicals are natural products which plants normally exude from their roots as defence and signal compounds. By learning how to elicit their production and then how to collect these molecules, PHI has opened up a new source of natural products for many applications, such as pharmaceuticals, flavours, fragrances, nutraceuticals, and so forth.

Annex 2.2

PULP AND PAPER

The pulp and paper industry is a large and growing portion of the world's economy. Pulp and paper production has increased globally, as has the rate of paper consumption. In general, the industry is very capital-intensive with small profit margins. This tends to limit experimentation, development, and incorporation of new technologies into mills. However, the pulp and paper industry is facing increasing pressure from environmental regulations. To keep up with the increasing demand for pulp and paper and to meet increasingly stringent environmental regulations, the industry has been constantly looking towards technological improvements. Over the past 20 years, research efforts in laboratories around the world have sought to apply biotechnology in industrial wood processing. This brief overview summarises different biotechnological applications of microbes and their enzymes in the pulp and paper industry which have been commercialised or are under development. It also offers a perspective on future developments.

BIOPULPING

Biopulping is defined as the treatment of lignocellulosic materials with lignin-degrading fungi prior to pulping. It is getting closer to commercialisation. In the 1970s, Eriksson and co-workers at the Swedish pulp and paper research institute (STFI), Stockholm, launched a fairly comprehensive investigation that demonstrated that fungal pre-treatment of lignocellulosic materials could result in energy savings and strength improvements for mechanical pulping. Mechanical pulping involves the use of mechanical force to separate wood fibres. Mechanical processes have high yield (up to 95 per cent) and produce paper with high bulk, good opacity and excellent printability. However, they are energy-intensive (electricity use) and produce paper with relatively low strength and high colour reversion rate (tendency to turn yellow with time). The pulps from several wood species have high pitch content and therefore require ameliorating steps. Although the STFI research had limited success (it encountered difficulties in scale-up), it provided valuable insights. A more comprehensive evaluation of biomechanical pulping was launched in 1987 at the US Departent of Agriculture (USDA) Forest Service, Forest Products Laboratory (FPL), under the auspices of a biopulping consortium. The consortium (April 1987-August 1996) involved the FPL, the Universities of Wisconsin and Minnesota, the Energy Center of Wisconsin, and 22 pulp and paper and related companies.

The consortium has established the economic feasibility of biopulping at pilot scale in connection with mechanical pulping. The two-week, environmentally friendly process increases mill throughput by 30 per cent or reduces the electrical energy requirement by at least 30 per cent at unchanged throughput. It also improves paper strength. Investigations at laboratory scale have sorted through the more than 30 variables associated with biopulping, including species and strains or fungi, inoculum form and amount, species of wood, wood chip size, environmental factors, effect of added nutrients, need to sterilise the chips, etc. Of several hundred species and strains of white-rot fungi examined to date, *Ceriporiopsis subvermispora* was found to be the best for both hardwood and softwood species. Recent research findings, aimed at commercialisation, include the following:

- brief atmospheric steaming of the chips (as short as 15 seconds) is sufficient to give the biopulping fungus a competitive advantage over indigenous microbes even in heavily contaminated chips;

- the quantity (cost) of the fungal inoculum can be reduced substantially by supplementing the fungal inoculum with a relatively inexpensive nutrient, corn steep liquor (a by-product of the corn wet milling process;
- chip pile temperature and moisture can be controlled with conditioned forced air, removing a substantial amount of fungal metabolic heat.

An engineering design for decontaminating wood chip surfaces, cooling the chips after steaming, inoculating them with the fungus on a continuous basis, and removing heat from the pile was successfully tested on increasingly larger scales. In October 1996, a 50-tonne (dry weight basis) outdoor chip pile experiment was conducted at FPL to test the design. Results were equal to laboratory-scale experiments. In July 1997, another 50-tonne (dry weight basis) outdoor chip pile experiment was performed successfully at FPL, and the chips from this trial were refined through a commercial thermomechanical pulp mill in Wisconsin.

An economic evaluation has been performed for a 600 tonnes/day thermomechanical pulp mill. The fungus treatment time was two weeks in a flat pile geometry operating in a northern climate. Capital costs to incorporate this biopulping technology into a paper mill are estimated to be between $5 and $7 million. Savings of $10 per tonne of pulp may be realised with 30 per cent savings in electrical energy. This is equivalent to an annual savings of $2 million, which, compared to the estimated capital costs, results in a simple payback period of two to three years. Mills that are refiner-limited may experience throughput increases of over 30 per cent from the reduction in energy by refining at a constant total power load. A 20 per cent increase in throughput results in savings of $55 per tonne of pulp or $12 million annually. With this improvement, the payback period for this technology is approximately six months. If 5 per cent of the kraft pulp is substituted by biomechanical pulps in a blend, an additional savings of over $13 per tonne of pulp may be realised.

Weaver Industries, Inc., Fresno, California, through its subsidiary, Biopulping International, Inc., Madison, Wisconsin, has taken the lead in commercialising biopulping technology. The principals of this company are promoting the technology world-wide and have developed an extensive technology package which includes the patent licensing arrangements, the supply of fungal inoculum, the design and supply of appropriate equipment, and most important, the technical know-how.

Studies mainly conducted in the United States, South Africa, Brazil, Austria, and India suggest that the fungal pre-treatment is effective on non-woody plants, and that it also benefits sulphite and kraft pulping processes, as well as organosolv and dissolving pulp production.

PITCH PROBLEMS

Pitch is the mixture of hydrophobic resinous materials found in many wood species and constitutes some 2-8 per cent of total wood weight, depending upon the species and the time of year. It causes a number of problems in pulp and paper manufacture, including deposits on tile and metal surfaces, plugging of drains, discoloration of the felt, tears and other defects in paper, downtime for cleaning, etc. Traditional methods of controlling pitch problems include natural seasoning of wood before pulping and/or adsorption and dispersion of the pitch particles with chemicals in the pulping and papermaking processes, accompanied by adding fine talc, dispersants and other kinds of chemicals.

During the past ten years or so, two biotechnological methods have been developed independently and are now been used industrially. In the late 1980s, scientists in Japan discovered that the treatment of mechanical (groundwood) pulps with lipases, which catalyse the hydrolysis of triglycerides, reduces pitch problems significantly. In the early 1990s, Sandoz Chemicals Corporation in the United States (now Clariant Corporation) introduced a new product for control of pitch in pulpwood chips, called Cartapip™. Cartapip™ is a fungal inoculum of the ascomycete *Ophiostoma piliferum*. A water slurry of the fungal spores is sprayed onto wood chips as they are piled prior to pulping. The fungus invades the wood cells, degrading the pitch. Pitch, including toxic resin acids, is also metabolised quite effectively by lignin-degrading fungi in biopulping, thus offering an additional benefit.

FIBRE IMPROVEMENTS OR MODIFICATIONS

The structure and chemical composition of pulp fibre surfaces are of paramount importance for paper strength and other properties. Due to the higher yields obtained with mechanical pulps as compared to chemical pulps, they have attracted growing interest. Sometimes chemical pulps are added to mechanical pulps to impart strength or other properties. With improvement of mechanical pulp fibre properties, the use of chemical pulps can be reduced or eliminated.

Enzymes have been used to improve physical properties of fibres and might have a commercial role in future. Cellulases can enhance pulp fibrillation and thereby improve paper strength. They can reduce fibre coarseness and increase paper density and smoothness. However, they reduce viscosity and must be used with care. Xylanase preparations have also been reported to improve pulp fibrillation and fibre bonding. With recycled fibres, there is growing concern about the rate of water drainage on the paper machine. The speed of paper machine operation depends in part on the drainage rate of water out of the pulp mat. Drainage rates tend to be lower for recycled fibres than for virgin fibres so that there is a decrease in the paper machine production rate as recycled fibre content increases. It has been discovered that cellulases and hemicellulases can improve the drainage rates of recycled fibres. Pilot and mill-scale testing has led to the commercial use of these enzymes as drainage aids. In the future, other enzyme-based processes could lead to cleaner and more efficient pulp and paper processing.

Starch-modifying enzymes are sometimes used to improve paper quality. Enzymatic modification of starches is a cleaner process than chemical (oxidative) modification, as less energy is used and less waste is produced. Enzymetically modified starches at the wet end (size press) are applied in about 10 per cent of paper production.

DEINKING

Traditional deinking processes use caustic soda, silicates and peroxide for deinking oil-based printing materials such as newspapers and magazines. However, with the growing use of coating and new types of inks containing synthetic polymers in laser and xerographic printing, conventional deinking methods are inadequate for producing high-quality pulps. Recycling mills are therefore increasingly dependent upon mechanical devices to break down the larger non-ink particles to allow for removal by floatation or washing. Enzymatic techniques that allow for deinking of all kinds of recycled papers have recently been developed and commercialised.

BLEACHING OF KRAFT PULPS

The kraft process accounts for most of the world's pulp production. Kraft pulping degrades and removes most of the lignin, without severely damaging the cellulose. Kraft pulps have a characteristic brown colour, which must be removed by bleaching before the manufacture of printing and writing or other products in which appearance is important. Kraft bleach plants use a variety of chemicals and treatment sequences to convert brown kraft pulp to white pulp. Traditionally, chlorination has been used, but because of consumer resistance and environmental regulations on chlorine bleaching, pulpmakers are turning to other bleaching chemicals (chlorine dioxide, oxygen, ozone, and peroxide), to extended pulping times (thereby lowering the pulp lignin content and decreasing bleaching chemical requirements), and to other process modifications. However, disadvantages associated with some of these methods are higher cost and/or greater danger of loss of pulp yield and strength as compared with chlorination.

A new method for whitening wood pulp has been developed at Haifa Technion in Israel and successfully tested in a large-scale paper mill trial. The essence of the process is a new enzyme better suited to the temperatures and pH found in pulp processing. The cost of the process is said to be the same as the conventional chlorine-intensive method. This is an example of the continuous improvement that characterises many biotechnological processes. The drawbacks of conventional enzymes have been overcome to make a step change in the competitiveness of the biotechnology-based process.

Studies conducted in Finland show that hemicellulases (mainly xylanases) enhance pulp bleaching. These enzymes are now being used commercially in Scandinavia, Canada, the United States, and Chile. The treatment of kraft pulps with xylanases leads to significant reduction in chemical consumption with almost no loss in pulp yield or quality. Biobleaching of acid bisulphite pulp with xylanases has also shown promise, with chemical savings of up to 51 per cent. Research is now being directed towards the discovery or engineering of enzymes that are more robust with respect to pH and temperature.

Ligninases such as manganese-dependent peroxidase and laccases have also shown potential in pulp bleaching, but have not been used commercially. Both of these enzymes can achieve more substantial delignifying action than xylanase, but there are obstacles to be overcome before either enzyme can be used cost-effectively. There is currently no large-scale commercial source for either enzyme, so costs remain to be established. Current efforts have been to produce these enzymes cheaply enough so that the technology can become economically attractive. Also, genetic engineering of a fungus to produce a desired mixture of enzymes and their cosubstrate *in situ* may become more cost-effective than producing and applying the enzymes in separate steps.

REDUCTION OF ORGANOCHLORINE COMPOUNDS IN BLEACH PLANT EFFLUENTS

Organochlorines have been a matter of concern in the pulp and paper industry for the last two decades. These compounds are produced mainly by the reactions between residual lignin present in wood fibres and the chlorine and chlorine derivatives used for bleaching. Some of these compounds are toxic, mutagenic, and persistent; bioaccumulation causes harm to biological systems. Earlier measures taken by the pulp and paper industry to solve the chlorine problem focused on improving effluent treatment methods. Many physico-chemical methods have been used to treat bleach plant effluents, including precipitation with lime, alum and metal ions, and synthetic polymeric coagulants; adsorption on activated carbon, natural clays and polymeric adsorbents; membrane techniques; rapid filtration in soil; UV irradiation; and oxidation using oxygen, sulphur dioxide, hydrogen peroxide and sodium hypochlorite. The problems underlying the physico-chemical treatments are those associated with cost and reliability. Today, R&D in this area has shifted towards improving the pulping process to decrease production of undesirable by-products.

Biotechnological methods have the potential to eliminate or reduce the problems associated with physico-chemical methods. Biological treatments with bacteria or fungi are known to be effective in reducing the biological oxygen demand (BOD), the chemical oxygen demand (COD), and the toxicity of kraft pulp mills. Some enzymes also seem to have the potential to remove colour and adsorbable organic halogens from pulp and paper mill effluents. Peroxidase, laccase, etc., are the most important of these. Many factors have to be considered in choosing an effective and commercial bleaching/treatment process that meets all the environmental guidelines. These processes are not used commercially.

The most widely practised of the earlier biotechnologies are waste treatment processes. These are based in large part on the degradative activities of mixtures of aerobic and anaerobic micro-organisms, primarily bacteria. Advances in wastewater treatment applications have been in the engineering rather than the biological aspects. As environmental controls become stricter (*e.g.* the US Environmental Protection Agency's "Cluster Rules"), it is likely that innovations will be made in biological as well as engineering aspects of wastewater treatment. It appears that the only long-term solution is to develop technologies that will allow mills to operate with zero effluent.

At present, cleaner production is largely achieved by process-integrated water treatment using biologically treated process water from the same production plant. Some 10-20 per cent of European paper producers reuse treated water in this way, so that there is zero discharge of wastewater (Hooijmeijer, personal communication). In the United States and Japan, a much smaller number of paper manufacturers use treated wastewater.

BIOFILM PROBLEMS

Biofilms (slimes) in pulp and paper mills are a serious problem. They clog wires, pipes, and drains and contaminate the product itself, sometimes to the point of discoloration. They are controlled primarily through the use of biocides, some of which can be toxic to humans and other life forms. A significant amount of research has gone into finding environmentally benign control methods. Because the biofilms are comprised of bacteria and fungi embedded in a matrix of extracellular polysaccharides, enzymes that hydrolyse the polymers have been studied. There is at least one commercial enzyme product, "ED-l", a levulanase used by paper mills in the United States, Scandinavia, the United Kingdom, and Japan. Another promising method of controlling biofilms is the introduction of non-film-forming microbes that outcompete the biofilm formers for substrates. It is likely that a combination of enzymes, friendly microbes, and dispersants will ultimately be used to lower or eliminate the use of biocides in pulp and paper mills.

THE FUTURE

From the foregoing, it is clear that several applications of biotechnology in pulp and paper processing have been commercialised and that others are under development. Basic discoveries are being made all the time, and it seems likely that some of the directions being pursued today will lead to major new applications. Developments in biocatalyst engineering are one example. Today's enzymes will be replaced by natural ones that are more robust in industrial processes, and these in turn will be replaced by enzymes designed for specific applications. It is likely, moreover, that catalysts based on enzyme-active sites, but not constrained by the fragility of protein structure, will be developed for a variety of applications. Use of whole micro-organisms in wood and pulp processing is likely to become increasingly attractive; biopulping, for example, has been shown to have great potential even without strain improvements via conventional breeding or genetic engineering.

It would be a serious case of negligence to fail to mention the tremendous impact that biotechnology will play in the production and quality of trees for pulp and paper and other uses. The power of biotechnology will continue to be applied to tree production and improvement. Superior lines will be produced by cloning, as has already been done with eucalyptus. Artificial seeds will be produced from desired individuals. Trees will be genetically engineered to have altered lignin or decreased lignin content, to flower early, to have superior fibre form and morphology, to have insect, pathogen, herbicide and pollutant resistance, and to produce valuable products. Indeed, some will probably be genetically tailored to facilitate bioprocessing.

Annex 2.3

METALS AND MINERALS

BIOLEACHING/MINERALS BIOOXIDATION

Stirred-tank biooxidation at Youanmi Mine, Western Australia

Youanmi Mine, owned and operated by Gold Mines of Australia, uses BacTech (Australia) Limited's thermophilic bacteria at 50-52 °C to process 120 metric tonnes/day of a flotation concentrate grading 60 g/t gold. The gold is locked in an arsenopyrite, which is degraded by the bacteria. Gold recovery ranges from 95 to 98 per cent. The capital cost of the biooxidation plant and associated washing and neutralisation circuit was $3.89 million. The operating cost is $37/metric tonne of concentrate treated.

Bioheap leaching of copper sulphide ore at Quebrada Blanca, Chile

Compania Minera Quebrada Blanca, operated by Cominco Limited, lies 4 800 m above sea level in the Andes of northern Chile. It processes 17 300 metric tonnes/day of chalcocite (Cu_2S) ore by bioheap leaching. The ore, crushed to 6 mm, is stacked on lined pads, and the bacteria extract 80-82 per cent of the copper. The copper exits the heap in the leach solution, which is processed by solvent extraction and electrowinning to produce 75 000 metric tonnes of cathode copper a year. It is the world's largest stand-alone bioheap leach operation. No effluents requiring treatment leave this plant. The capital cost of $360 million includes the total investment for the mine, including development and infrastructure. The operating cost is less than $1.10/kg of cathode copper.

Minerals ''biooxidation'' refers to a pre-treatment process which uses the same bacteria as bioleaching to catalyse the degradation of mineral sulphides, usually pyrite or arsenopyrite, which hosts or occludes gold, silver or both. In biooxidation, the values remain in the solid phase, and the solution is discarded. The solids are washed with water, neutralised with lime, and treated with a dilute solution of sodium cyanide or other lixiviant to solubilise the precious metals.

Bioleaching and minerals biooxidation are applied in:

- Aerated, stirred-tank reactors to process mineral concentrates. The reactors are stainless steel tanks and the process involves a series of three or more stages. The first has several tanks in parallel. Air is injected into the tanks and each tank is equipped with an agitator to break up air bubbles and promote uniform suspension of solids. Because of the heat generated from the oxidation of sulphide minerals, the reactors are cooled with water jackets or cooling coils.
- Bioheaps to process ores. The ores are crushed and stacked on lined pads, and the sulphide minerals are leached with an acidic ferric iron solution containing the bacteria. For base metal ores, the product of value is in the leach solution exiting the heap. For precious metals, the biooxidised ore is washed with water and the biooxidised ore is mixed with lime and restacked for treatment with a dilute cyanide solution to extract the metal.
- Processing of base metal ores in the ground. This process is similar to bioheap leaching except that the ore is fractured *in situ* using explosives, and the leach solution and bacteria percolate into the fractured ore body. The solutions containing the metal of value are collected at the base of the ore body and pumped to the surface for metal recovery.

Metals bioremediation and recovery

Micro-organisms immobilise, mobilise, or transform metals by extra-cellular precipitation reactions, intracellular accumulation, oxidation and reduction reactions, methylation and demethylation, and extra-cellular binding and complexation. Microbial processes which have been extensively pilot tested or are commercially used are:

- Extra-cellular precipitation, which uses the sulphate-reducing bacteria to produce hydrogen sulphide to precipitate heavy metals as insoluble sulphides. The metal sulphides are reclaimed. The organisms also produce bicarbonate ions that assist in neutralising acidic waste streams.
- Extra-cellular binding and complexation, which uses micro-organisms to concentrate metals on the outside of the microbial cell. Micro-organisms, whether living or non-living, possess an abundance of function groups on the cell surface that bind metal ions. These functional groups contribute a net negative charge to the micro-organisms. Positively charged metal ions are bound to the cell wall of the micro-organisms by adsorption type reactions, metal reduction, complexation reactions, and precipitation type reactions. The metals can be stripped from the micro-organisms by acid or chelating agents and reclaimed for reuse.

Annex Table 2.1 summarises the major successful bioreactor plans (as well as some under development) for pre-treatment of gold concentrates prior to gold recovery by cyanidation. Starting dates, scale expansions, and some plant capacities are indicated. The different ratios of mineral feed and tonnages and sulphur oxidised reflect the different compositions of minerals.

Annex Table 2.1. **Bioreactor plants for pre-treatment of gold concentrates**

Location	Operating period	Mineral (tpd)	Sulphur (tpd)	Total capacity (m^3)
Fairview, South Africa[1]	1986-91	10		
	1991-to date	35	7	900
São Bento, Brazil[2]	1990-95	150	24	
	1995-to date	110		1 160
Harbour Lights, Australia[3]	1991-93	40		
Wiluna, Australia	1993-96	115		
	1996-to date	152	36	4 240
Youanmi, Australia[4]	1994-to date	120		–3 000
Sansu, Ashanti, Ghana[5]	1994-95	720		
	1995-to date	1 152	127	21 360
Tamboraque, Peru[6]	–	60	18	1 572
Amantaytu, Uzbekistan[7]	–	1 100	275	23 376

Tpd = tonnes per day.

1. The success of a pilot trial at Fairview between 1984 and 1986 led to commissioning of this first commercial bioreactor, which, on its expansion, replaced the more traditional roasters used at the site.
2. The expansion at São Bento, where concentrate is partly oxidised biologically before passing to autoclaves for pressure oxidation, represented the halfway stage to a planned four reactors. Expansion in bioreactor capacity was more cost-effective than increasing pressure oxidation capacity. A reduction in tonnage treated reflects a process design change to more extensive biooxidation of the sulphide (70 per cent instead of the 30 per cent design value).
3. The short life of this plant was related to the need to treat a limited stockpile of concentrate.
4. Using Bactech's moderately thermophilic bacteria at about 50 °C. This is the only gold mineral treatment plant listed in this table not to use the BIOX® technology developed by Gencor (Billiton SA Ltd. Process Research), South Africa.
5. Now four modules, each comprising six reactors. The expansion took concentrate that would have been destined for a roaster.
6. Under construction.
7. Awaiting financial support.

Source: Norris, personal communication.

Metals recovery

A zinc refinery in Budel-Dorplein, the Netherlands, has the largest commercial bacterial sulphate reduction project for removing metal contaminants from groundwater. Commissioned in 1992, the plant is designed to treat 300 m^3/hr of effluent containing 100 mg/l zinc, 1 mg/l cadmium, and 1 000 mg/l sulphate. The microbial treatment process, commercially developed by Paques Biosystems International B.V. (Balk, the Netherlands) and Paques, Inc. (Exton, Pennsylvania), achieves an effluent discharge of <0.3 mg/l zinc, <0.01 mg/l cadmium and <200 mg/l sulphate. The metal sulphides, precipitated by the H_2S, and elemental sulphur, produced from microbial oxidation of excess H_2S, are returned to the smelter where the metals are reclaimed and the sulphur is converted to sulphuric acid in the acid plant. Total costs (chemicals, energy and depreciation) of a microbial sulphate and metals removal facility depend on waste stream characteristics and discharge criteria. However, as an example, the estimated cost for a plant reducing 10 000 metric tonnes/yr sulphate would be about $330/metric tonne sulphate.

MARKET PENETRATION AND TRENDS

Bioleaching/minerals biooxidation applications are now evaluated along with competitive technologies for nearly all new mining projects around the world. Several technology companies and a handful of qualified consultants market the technology and several major global engineering companies design and engineer the systems. Technical papers and short courses on the technology are given at major international mining conferences and trade shows. Many mining companies, wishing to understand and apply the technology, hire consultants and/or engineering companies to teach them about the processes and to assess possible applications throughout the companies' operations.

Biological sulphate reduction for metal recovery is a lesser-known technology. Only one company markets the technology; it markets it world-wide through technical presentations and site visits to prospective customers. Co-operative agreements with other technology companies are being considered, and this should expand marketing efforts. Many mining companies are committed to becoming more aware of biotechnology applications, and this will certainly enhance sales of sulphate reduction technology.

POLICY CONSIDERATIONS

Neither bioleaching/mineral biooxidation nor sulphate reduction technology for metals recovery is substantially affected by existing policies. Genetic engineering is being studied at a very fundamental level for bioleaching, but commercial applications are likely to be a decade or more away.

ECONOMIC ANALYSIS

Closed biological reactors are used for recovering metals, especially gold. However, as the sales value (BRS – biotechnology-related sales, as defined in Chapters 1 and 2) of the biotechnology industry in this sector is very small, market penetration cannot be assessed as yet (Abbott, 1996). About 25 companies now produce gold using this biotechnological process. It can generally be said, however, that minerals and metals do not lend themselves to biological conversion; the application of biotechnological processes will therefore always be limited when compared to physico-chemical processes. Biotechnology will play a role in end-of-pipe technology, which is not considered part of clean technology, unless it provides integrated water reuse. This has not yet been achieved in the metals and mining industry on a large scale.

THE ECONOMICS OF BIOLEACHING

Some 25 companies now use biotechnology to recover gold from ore concentrate. The biotechnological unit operation has been compared with the two main alternative physico-chemical unit operations in terms of competitiveness (McNulty and Thompson, 1990), and some preliminary indications of the environmental benefits can be given.

Since gold became a free market commodity in the mid-1970s, it has attracted continuous interest. Its value exceeds its production costs, and, in the United States, gold production grew from 1 million troy ounces to 5 million troy ounces in 1987 and was then still increasing.

There are three principal techniques for pre-oxidation of the refractory gold ores: roasting, aqueous pressure oxidation, and microbial oxidation. Roasting has some negative environmental impacts, *i.e.* high energy use, and gas emissions, which necessitate gas cleaning equipment (high investment and operating costs). Also, the subsequent cyanide leaching may have a yield as low as 80 per cent. Pressure oxidation is conducted at temperatures of 180-210 °C. This requires a high energy input and costly investment in high-pressure equipment. The yield in the cyanidation process is high, typically over 90 per cent. The biotechnological process does not require high investment and operating costs, as it does not involve high temperature or pressure, and there is thus an environmental gain in terms of reduced carbon dioxide emissions. In fact, the bacteria involved consume carbon dioxide to produce biomass. Some energy is needed for cooling purposes. On the other hand, residence times in the reactor are much longer. Annex Tables 2.2 and 2.3 compare the costs of these three pre-oxidation technologies.

Annex Table 2.2. **Estimated plant operating and investment costs for refractory gold ore in a 100 tonnes per day pre-treatment plant**

Item	Roasting	Pressure oxidation	Bacterial oxidation
Investment costs (thousand $)	4 370	3 380	2 490
Total operating costs (thousand $/yr)	1 580	1 440	1 510
$/tonne concentrate	45.10	41.10	43.10
$/tonne ore	4.50	4.10	4.30

Source: McNulty and Thompson, 1990.

Annex Table 2.3. **Economic comparison of three metal recovery units**

Item	Roasting	Pressure oxidation	Bacterial oxidation
Investment costs (thousand $)	16 800	15 600	14 430
Total operating cost $/tonne	13.60	13.20	13.40

Source: McNulty and Thompson, 1990.

As the data presented in these tables show, the three factories refining gold from refractory ores using the three processes have very similar operating costs, but the investment costs for the biotechnological process seem to be substantially lower than for the physico-chemical processes. The choice of biotechnology applications will depend not only on the costs, however, as the biotechnological process is not yet a proven technology and will not be suitable for all ores.

Annex 4.1

LCA METHODOLOGY

DEFINITION OF THE AIM AND SCOPE OF THE STUDY

The first task of an LCA is to define the aim and scope of the study and to tailor it to its intended application. It should be borne in mind that the scope of the study should be designed so that the aim and intended application can be achieved. An exact description of the reasons for carrying out the intended LCA and of the target groups to be reached is the first priority. The aim should define the questions to be answered. This is necessary, among other reasons, so that the necessity and relevance of each stage of an LCA can be reviewed in the light of the information it yields. More exacting demands can be made of LCA studies to be used for political decision-making processes, which can have far-reaching consequences for the economic sectors concerned, than for in-house analyses of shortcomings.

In order to give a clear and exact description of the system to be studied, a number of definitions must be given at the very outset. The most essential are:

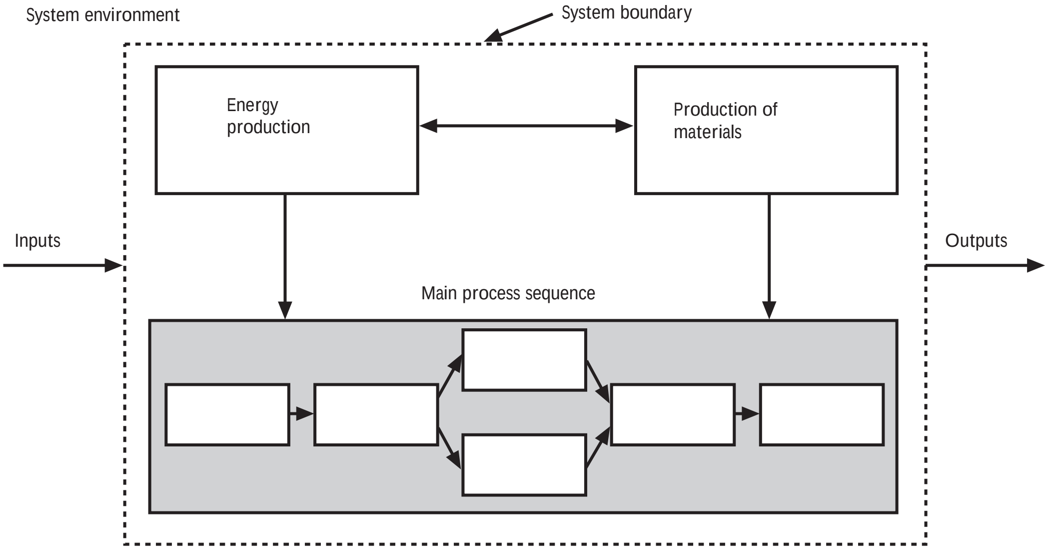
- the functions of the system and the functional unit;
- system boundaries;
- allocation procedures;
- the types of impact to be addressed;
- the methodology of impact assessment and subsequent interpretation;
- data requirements;
- assumptions and limitations;
- the accompanying critical review, if applicable;
- type and structure of the LCA report, if applicable.

The definitions should not be regarded as static, but as modifiable at any stage of the study as additional information is collected.

A functional unit is a measure of the performance of the system studied and has to be clearly defined and measurable, *e.g.* 1 000 l milk packed and transported, or 1 m^3 enclosed space. The functional unit provides a reference for all the inputs and outputs. It establishes the functional equivalence of two systems that are to be compared and is consequently indispensable for guaranteeing comparability of results. For example, if the systems to be compared, A and B, each fulfil functions x and y, but A also fulfils function z, function z must also be documented. Another method is to add a system that fulfils function z to B.

The term "product system" means the combination of the processes, linked by material and energy flows, that fulfil one or several pre-determined functions. The system boundaries represent the interface between the product system under consideration and the environment or other product systems. Consequently, system boundaries determine the processes that are to be the subject of an LCA study (Annex Figure 4.1). The system should be modelled so that input and/or output at the system boundaries can be represented as basic flows, *i.e.* they can either be removed from the environment without pre-treatment or discarded without post-treatment.

◆ Annex Figure 4.1. **Boundaries of a product system for an LCA study**



System boundaries depend on many factors, particularly application, target group, assumptions made, cut-off criteria, data, and cost constraints. As the boundaries can considerably influence the results of an LCA, the criteria used to determine them should be described and justified. The system should be described with sufficient detail and clarity to allow a third party to reproduce the inventory.

The quality of the data compiled for the inventory can considerably affect the thrust of an LCA. The objectives and scope of the study generate requirements concerning the quality of the data, which encompass both their quantitative and qualitative aspects and the methods used to gather and process them, such as:

- geographical, technical and time-related coverage;
- completeness, exactness and representative quality;
- unreliable and variable nature of the information;
- consistency and reproducibility of the methods used in the LCA;
- reproducibility of the results by an independent third party.

It has to be decided to what extent the LCA necessitates a survey of specific data, *i.e.* from actual firms with defined processes and transport routes, or whether estimates or general data from the literature can be regarded as adequate. In practice, a combination of measured, calculated and estimated values is generally used, with more weight given to plant-specific data than to general data from the literature. For practical reasons, however, it is only rarely possible, within the scope of an LCA, to conduct large-scale measuring campaigns for data acquisition purposes. Transparency can be guaranteed by citing the sources of all data used.

With industrial processes, depending on the technical standard of the individual plant, the data available for identical processes often vary greatly. Particularly in the case of comparative studies, the use of different types of data, *e.g.* actual state, technical optimum, and international mean values, can result in considerable differences in data and thus in erroneous conclusions.

In order to expose contradictions and gaps in the data, the data acquired should be subjected to a validation procedure. Both mass and energy balance sheets, as well as comparative analyses of emission factors are suitable for this purpose. With biotechnical processes, this can give rise to problems, as processes are often not constant. In addition, they often use small quantities which are consequently difficult to determine.

If an LCA is carried out jointly with an industrial company, available data can be an important basis. Problems and gaps in the data often arise for processes outside company premises. Then data published under data protection conditions (*e.g.* by applying average values) have to be used. Despite efforts by various national and international bodies, *e.g.* SPOLD (Society for Promotion of Life Cycle Assessment Development), there is an evident lack of generally acceptable data.

When comparing product systems, comparability of the systems investigated must be ascertained. This means the ability to use the same scope and parameters (functional unit, system boundaries, data quality, allocation procedures, criteria for assessing input and output flows, and criteria for impact assessment). Differences among the systems have to be identified and reported. If comparisons are to be published, it is imperative to apply the impact assessment step in accordance with the ISO draft (see Annex 4.2). Moreover, the methods applied should be reviewed by an independent advisory committee. Great caution should be used when making comparative assertions without prior impact assessment, as inventory results rarely prove the absolute superiority of a system.

INVENTORY

An inventory is made by collecting data from the relevant inputs and outputs: use of energy and resources, emissions into environmental media (water, soil, air). If necessary, the data are then quantified mathematically. If the goals of the LCA studies match, interpretations may be made from these data. An exhaustive analysis of a product's life cycle has to take into consideration not only the mass and energy flows related to raw materials acquisition and production processes, but also those related to transportation, use and disposal. When comparing the production of homogeneous products, the latter group is generally of less significance. Nevertheless any omission of life cycle stages, processes or environmental pollution should be justified.

In order to determine a system's input and output, the system must be broken down into individual production processes (see Annex Figure 4.2).

In practice, there may be several reasons why pollution caused by various product systems cannot be clearly differentiated, so that there are difficulties in ascribing different types of pollution to the various systems.

The simultaneous production of two or more products (A and B) by a single process (coupled production) is a case of this type. Product A is not entirely responsible for the pollution resulting from this process, as product B also benefits from the process and has its own market value.

Similarly, in a system for product A, material flows may not leave the system as waste, but be used in a system for product B (open loop recycling). The same is true if the system for product A, which is under consideration, uses recycled products from the system for product C, which is not.

The literature takes fundamentally different approaches to these questions (Klöpffer, 1996): scientifically exact and unquestionable approaches, independent of their practicability; or simplified rules which, although to a certain extent arbitrary, are applicable even to complex systems.

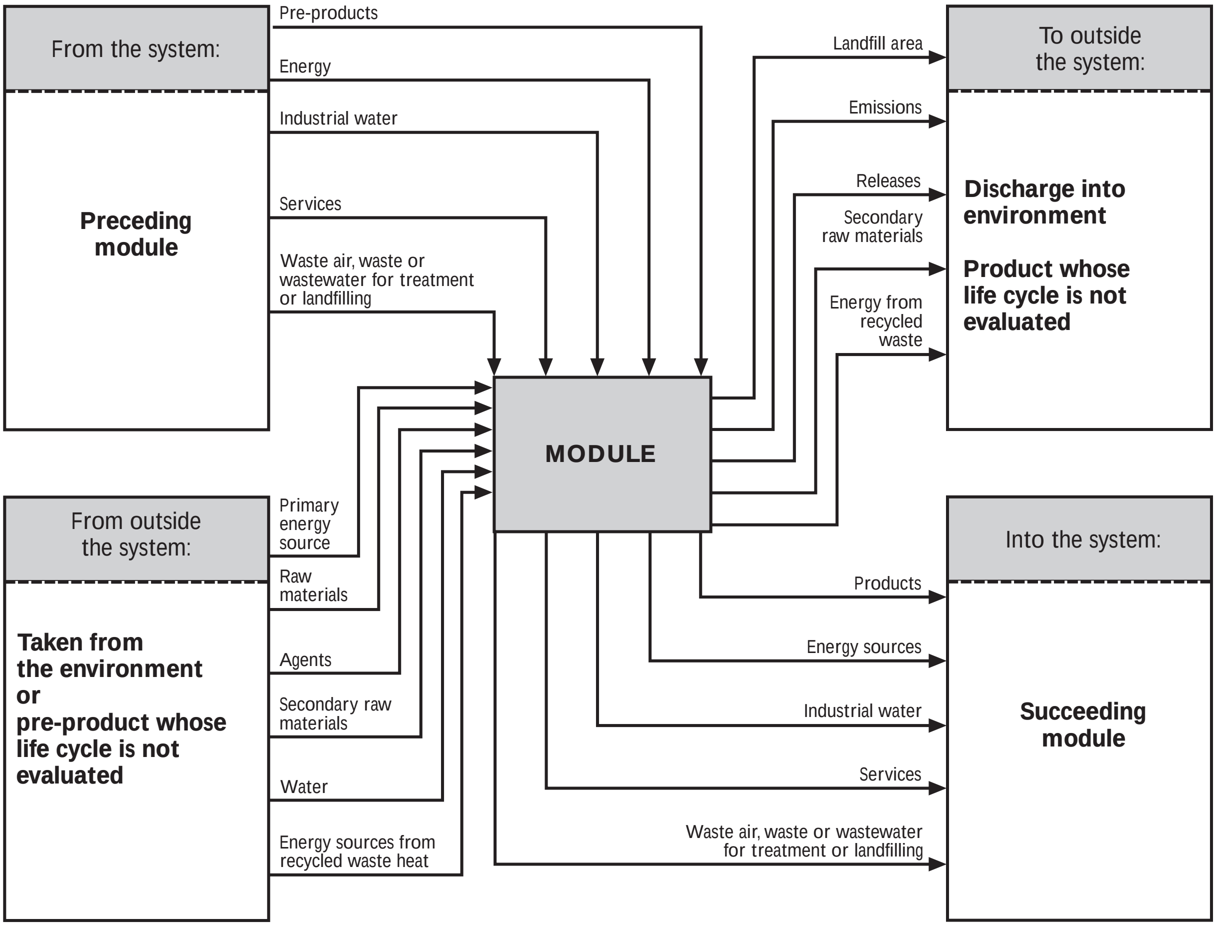
The most far-reaching scientifically exact approach is the extension of system A (under investigation) to include system B (and, if applicable, C). For complex systems, this procedure can result in such a proliferation of systems to be studied that an LCA is no longer feasible.

The following criteria should be applied for simple but plausible results:

- mathematical correctness, internal logic, no double counting of environmental impacts;
- feasibility when there is little information on use or origin of secondary raw materials;
- ''fair'' allocation (classification) of credits or debits with regard to producers and consumers of secondary raw materials.

In practice, there are often limitations on the labour-intensive task of data acquisition. In the course of an LCA, unavailable data and/or limited access to data and lack of time and capacity can mean that not all inputs and outputs will be measured. Therefore, it must be decided which processes should be investigated and in what detail. The aim is to determine essential material flows in a reasonable

◆ Annex Figure 4.2. ***Life cycle inventory analysis***



Source: Projektgemeinschaft Lebenswegbilanzen, 1992.

amount of time and effort, and this information is gained during the study in an iterative process. Material flows can be differentiated according to mass, energy or environmental categories:

- mass flows whose accumulation contributes a certain percentage to the mass balance of the product system under investigation;
- mass flows whose accumulation contributes a certain percentage to the energy balance of the product system under investigation;
- mass flows which contribute a certain percentage to a category of data under investigation, *e.g.* CO_2 emissions.

For comparative studies intended for publication, these various approaches should be compared via a sensitivity analysis.

Unlike the above-mentioned physical values, economic factors, such as the market value, are at a disadvantage as a reference, in that they are subject to severe market fluctuations.

IMPACT ASSESSMENT

With regard to the inventory, a consensus on procedure is gradually taking shape despite a few unresolved questions relating to methods and practical matters. The same cannot be said of impact assessment. Over the past few years many methods of assessing impacts have been developed. The function of impact assessment is to examine the data collected and, if applicable, aggregated in the inventory (mass and energy flows, environmental releases, etc.) for their possible environmental consequences. It is widely accepted that the areas to be protected are human health, the natural environment, and resources.

Life cycle impact assessment is composed of several individual elements (ISO 14042, 1997): category definition, classification, characterisation, and weighting. For each element, there is a specific procedure and set of methods; the assumptions and value choices can be made more transparent by clearly distinguishing among the elements.

The first element, definition of categories, identifies the particular categories that the LCA will address. Classification assigns inventory data to these categories. Characterisation involves an effort to determine and quantify the potential effects within individual impact criteria. Where possible, Life Cycle Impact Assessment (LCIA) aims to take a quantitative approach, but in some cases, value judgements are used to define categories and develop category models. Weighting results in a comparison of systems across the categories. Weighting is the most disputed part of an LCA, as it is not based on scientifically verified and/or generally recognised rules. A variety of procedures have been developed, each with their own specific advantages and disadvantages.

For weighting, principles, rather than individual methods, should be discussed, as weighting is strongly connected with values and is thus characterised by subjective elements. The assessment process that accompanies the weighting can be described as "the interlinking of available information pertaining to a set of given facts with a personal value system to form a judgement about the facts themselves" (Giegrich *et al.*, 1995). It would, therefore, be misleading to speak of an "objective weighting". This does not mean, however, that weighting is necessarily arbitrary. It is crucial that all the issues involved should be presented so clearly and precisely that outsiders cannot fail to understand them. The origin of the underlying values of the weighting may be: expert opinions (ascertained, for instance, by panel methods); political directives and aims; individual opinions of members of the public.

It is evident that different subjective values may lead to fundamentally different judgements on the same issue. Annex Table 4.1 provides a compilation of the many demands made of impact assessment methods. It should be emphasised that neither existing nor future procedures will be in a position to fulfil every requirement, particularly as the requirements themselves are not totally free of contradictions.

Annex Table 4.2 is a systematic representation of existing interpretation approaches; the largely subjective elements are indicated by italics.

Various impact assessment procedures have been compared, on the basis of emissions and interference with the global environment (see Figure 4.2 in Chapter 4). The comparison reveals a wide range of priorities, partly due to the different methodologies and partly to the use of different sets of data for weighting. The different methods do not all seek the same goals, and this automatically results in differences in impact assessment. However, it can be shown that most impact assessment methods can describe over 90 per cent of global impacts using a relatively small number of emissions or resources. High priority is often given to global warming and ozone depletion and low priority is generally given to use of land. The Landbank Panel places extremely strong emphasis on global warming (over 80 per cent) and the EPS method on use of resources (approximately 70 per cent). Such a clear setting of priorities should be subjected to close scrutiny.

The degree of comprehensiveness, the selection of environmental impacts to be assessed, and the methods to be employed depend on the objective and scope of the LCA. The various approaches to impact assessment can be divided into three groups: methods pertaining to impact categories and potentials; methods pertaining to weighted emissions of environmental media; methods pertaining to overall impact parameters, such as energy consumption and material intensity.

Annex Table 4.1. **Requirements for impact assessment**

Comprehensiveness	Interprets all *relevant* impacts on, or interference in, the environment (not all that occur) Addresses ecological scarcity in some form Includes the interests of all concerned with the product evaluation
Transparency	Is easy to understand Is communicable Explicitly mentions the weighting criteria used Addresses uncertainties Explicitly performs all weighting phases and presents results Presents the findings of the individual weighting phases Uses terminology adapted to the target group The result should be reproducible
Content	Independent, reliable results from short-term discussions Temporal and spatial aspects are suitably addressed Inclusion of dynamic elements for possible prognosis Scientifically sound, justifiable assumptions The assessor may introduce personal weightings Reflects the subjective nature of the weighting in general Is quantitative if possible but also permits qualitative aspects Includes as much scientific information as possible Addresses combined effects in some way The unit of the impacts (e.g. kg) should not affect the weighting
Feasibility	Leads to clear findings Is standardised Performable in a short time on a low budget Effective control instrument Weighting principles are kept simple and understandable Weighting factors are stable Uses single scores or indicators for communication

Source: Hofstetter, 1996.

Annex Table 4.2. **Approaches linking information to value systems**

Method	Brief description	Example
Utility value analytical approach	Formulation of criteria *Weighting* of criteria *Assignment of degrees of goal achievement* Mathematical calculation	VNCI, Netherlands
Loss-benefit approach	List of individual aspects *Assignment of one-dimensional values* for loss/benefit Sum of the values	EPS, Sweden
Critical quantities/ecological scarcity	List of individual aspects *Definition of critical quantities/material flows* Calculation of critical volumes/flows Sum of the values	BUWAL, Switzerland
Verbally argumentative	List of individual aspects *Discursive consideration* by value arguments Derivation of the impact assessment	UBA, Germany

Source: Giegrich *et al.,* 1995.

Methods pertaining to impact categories and potentials

There is a consensus that the following impact categories require consideration: depletion of resources; global warming; ozone depletion.

Other categories that are the subject of ongoing discussion include: formation of photochemical oxidants ("summer smog"); acidification; nutrification; human toxicity; ecotoxicity; decrease in diversity of species; odour; noise; land use; and risk of accidents.

The question of which categories should be considered is related to the feasibility of the characterisation, *i.e.* the quantification of the potential impacts. Global warming and ozone depletion clearly concern *global* impacts which can be satisfactorily estimated from the loads collected for the inventory. By contrast, photooxidants, acidification and nutrification are regional in nature and, according to type and extent, can cause different impacts, depending on regional circumstances. Spatial aspects are normally not part of an LCA. While different characterisation methods are available for these categories, this area requires further study.

Conclusive impact assessment of human toxicity, ecotoxicity, biodiversity, noise, odour and land use lies in the distant future. Approaches differ in particular with respect to incorporation of distribution and depletion parameters of individual substances. Problems are caused especially by insufficiently checked toxicity data and by lack of data on depletion behaviour and on intermediate products and by-products of the depletion.

It can be stated categorically that the goal of an LCA is not to determine the impacts *actually* caused by a product according to these categories, because in many sectors the scientific principles and corresponding data are simply not available. The assessment refers to *potential* environmental impacts from the stressors determined in the inventory. Stressors are conditions that can adversely influence the above-mentioned categories. If a stressor, such as NO_x, affects several categories, it will be examined several times. Even when the potential impacts are assessed, there are considerable uncertainties, as the example of global warming in Annex Table 4.3 shows.

Annex Table 4.3. **Structure of potential environmental impacts**

Rank	Example	Means of quantification
Primary	Change in absorption in infrared (IR) area	IR absorption and persistence of gases
Secondary	Change in global temperature	Complex calculations dependent on scale
Tertiary and higher	Changes in climate and ecological consequences	Determination of consequences difficult to perform

Source: Nordic Council of Ministers, 1992.

With regard to the quantification of impacts, various concepts exist, according to which the demand for data rises from 1 to 5 and feasibility within the scope of an LCA falls (Klöpffer and Renner, 1995):

1. addition of pollution as loads;
2. determination of load-related equivalence factors;
3. aggregation according to inherent chemical material properties, such as toxicity, persistence and bioaccumulation;
4. general assessment of stressor-effect linkage;
5. site-specific assessment.

According to the Dutch method, interference with the environment, partly in terms of material properties and partly in terms of generally valid models, is closely associated with potential environmental impacts. For classification and characterisation purposes, 15 impact categories were created (Annex Table 4.4). All are the object of international laws or agreements for the protection of the environment, such as the Rio Declaration, Agenda 21, or the Montreal Agreement.

Annex Table 4.4. **Impact categories of the Centre of Environmental Science, Leiden (CML)**

Impact category	Unit	Classification factor
Depletion of abiotic resources	–	1/reserves
Depletion of biotic resources	a^{-1}	BDF
Global warming impact	kg	GWP
Ozone depletion	kg	ODP
Human toxicity	kg	HCA, HCW, HCS
Aquatic ecotoxicity	m^3	ECA
Terrestrial ecotoxicity	kg	ECT
Formation of photochemical oxidants ("summer smog")	kg	POCP
Acidification	kg	AP
Nutrification	kg	NP
Waste heat via wastewater	MJ	1
Odour pollution	m^3	1/OTV
Noise	Pa^2*s	1
Damage to ecosystems and landscape	m^2*s	1
Victims (human)		1

Abbreviations used:

BDF	biotic depletion factor
GWP	global warming potential
ODP	ozone depletion potential
HCA	human toxicological classification factor (atmosphere)
HCW	human toxicological classification factor (water)
HCS	human toxicological classification factor (soil)
ECA	ecological classification factor for aquatic ecosystems
ECT	ecological classification factor for terrestrial ecosystems
POCP	photochemical ozone creation potential
AP	acidification potential
NP	nutrification potential
OTV	odour threshold value

Source: Heijungs, 1992.

For the characterisation and quantification of the contribution of material flows to the impact categories, calculation formulae for all the categories are given in the following form:

$$\text{Aquatic ecotoxicity } [m;^3] = \Sigma_i\ ECA_i\ [m^3/mg] \times \text{emissions}_i \text{ in water } [mg]$$

This method of quantification is frequently debated; however, to date, generally recognised characterisation methods have been available only for global warming and ozone depletion.

Methods pertaining to weighted emissions of environmental media

In the earlier days of LCA, the Swiss method of critical volumes was frequently used (Ahbe *et al.*, 1991). The weighting proceeds by means of existing, substance-specific limiting values for every substance *i:*

$$\text{Critical volume}_i\ [m^3\ ] = \text{emission load}_i\ [mg]/\ \text{limiting value}_i\ [mg/m^3]$$

Individual weighted emissions in the environmental categories water and air are then added together. The critical volume thus represents the – purely theoretical – volume of unpolluted air or unpolluted water that would be polluted by the emission load of the product system under study up to the observance of the limiting values. It is by no means intended to imply that exhausting the existing limiting values is considered desirable. In addition to the critical volumes of water and air, this method yields both the energy equivalence value (MJ/kg) and the volume of solid waste (cm^3/kg).

The sum of the quantities of critical air or water of all the emitted substances in one compartment should reflect its pollution and should be used for the evaluation. The criticism levelled at this method, which from a feasibility point of view is optimal within the scope of an LCA, is four-fold (Klöpffer and Renner, 1995):

1. As a rule, limiting values are oriented towards human health rather than towards toxicity.
2. Limiting values are not strictly scientific, but usually represent a compromise between protection, measurement and reaction engineering aspects.

3. Limiting values for one and the same substance can differ considerably from country to country.
4. For many substances no limiting values are available, although this does not make it possible to deduce the ecological safety of the substance.

Methods for overall impact parameters

Overall impact parameters have been developed which select energy and mass as reference points. These are somewhat simplified LCA studies which can nonetheless provide important information and indicate cases of severe pollution. Strictly speaking, energy consumption does not constitute an environmental impact, although it is recognised as a crucial environmental problem area. Environmental pollution linked to energy provision and distribution has a tremendous influence on the animate and inanimate environment.

Energy equivalence value, or accumulated energy consumption, has been collected in many inventories. It represents the energy assessed according to the necessary consumption of primary energy. As a rule, this is given in megajoules (MJ) and includes all the types of process energy and the inherent energy of the substances applied. In order to keep loss of information to a minimum, process energy, inherent energy and electric energy (given in kwh) can be reported separately. The same holds for energy from renewable raw materials, which can then be taken into account when calculating the global warming potential. If the energy equivalence value/accumulated energy consumption is also incorporated as an impact category, it should be noted that a number of the pollution factors relating to energy use are also taken into consideration in other impact categories, so that some values are duplicated.

The underlying principle of the material intensity per service unit (MIPS) concept derives from the insight that, in industrialised countries, the material flows in circulation have to be reduced if pollution is to be counteracted effectively. Experience has led to the conclusion that a more mass-intensive product causes more serious pollution than a comparable, less mass-intensive product, even though it fulfils the same function. The reason is that every movement of large material flows, whether for the production of raw materials or of energy, is inextricably linked to corresponding environmental repercussions (Schmidt-Bleek, 1993).

The implication of the MIPS method is, therefore, that the material intensity of processes or products per service unit produced can be used as an overall measure of environmental impacts. For this purpose, the quantities of all input flows covering the whole life cycle of a product have to be determined and aggregated. The inventory portion of a “comprehensive” LCA contains the data required.

Considered in isolation, the MIPS concept takes a purely quantitative approach. When toxic substances appear, this can lead to misinterpretation of anticipated environmental impacts. This explains why this method is currently the subject of intense discussion. Its advantage is that it does not depend on relatively uncertain process output data but works solely on the available input flows.

INTERPRETATION

In the interpretation, the results of the inventory, the assessment of impacts, or a combination of the two, are summarised in line with the defined goal and the scope of the LCA. Thus, the interpretation can be used, for example, to analyse internal shortcomings or as a decision-making tool. Interpretation comprises three steps (ISO 14043, 1997):

- identification of the most important inputs, outputs and potential impacts;
- evaluation, which involves three elements: comprehensiveness check, sensitivity analysis check and consistency check;
- conclusions, recommendations and reporting.

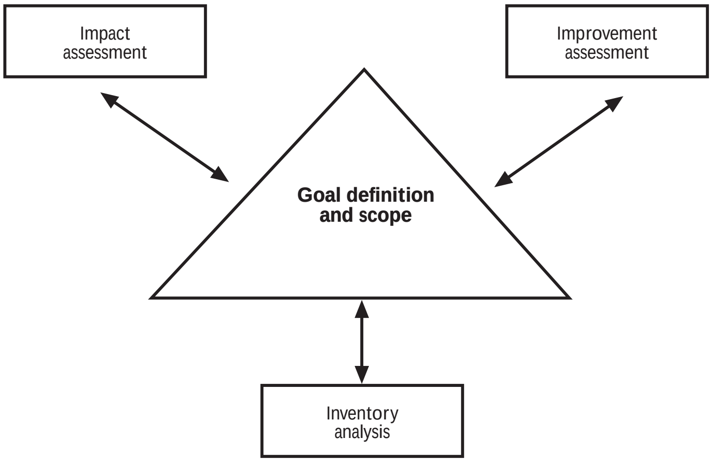
To summarise, the LCA is a tool that supplies valuable information for preparing and supporting decisions. However, the idea that LCAs could more or less determine (political) decisions is not valid.

Annex 4.2

LCA STANDARDISATION

Various studies have attempted to lay down at least the most important parameters. The first results, involving work schemes and methodology, were published in 1993. The Society of Environmental Toxicology and Chemistry (SETAC) published its concept in its Code of Practice (Annex Figure 4.3).

◆ Annex Figure 4.3. ***SETAC guidelines for Life Cycle Assessment***

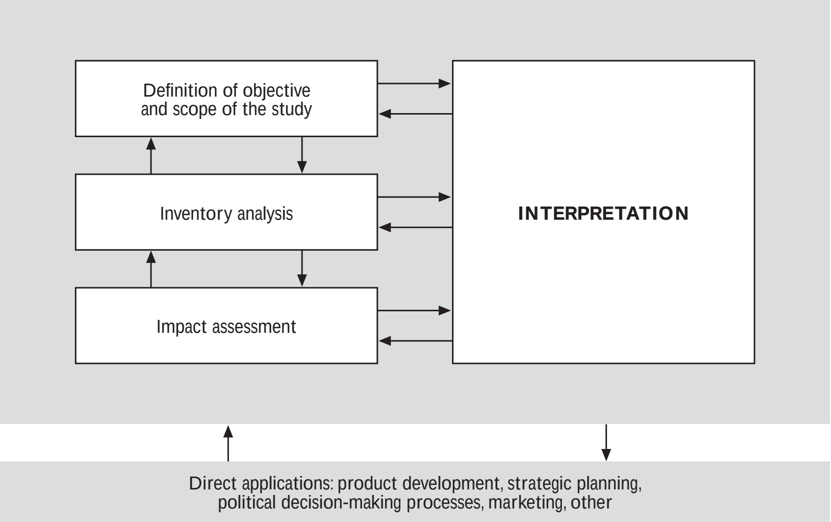


Source: SETAC, 1993.

The technical committee ''Environmental Management'' (TC 207) of the International Organisation for Standardization (ISO) is currently working on ISO standards for LCAs. The components of the ISO concept are indicated in Annex Figure 4.4.

LCA consists of four steps: definition of goal and scope, inventory analysis, impact assessment and interpretation. A life cycle inventory (LCI) omits the impact assessment step. The application of an LCA, *e.g.* to support the decision-making process in industry and government in setting priorities, or to assist strategic planning, product and process development, does not fall within the scope of the LCA itself. This also holds for socio-political and economic decisions. If, for technical or economic reasons, one of several competing products has overwhelming advantages, an LCA will normally be unnecessary.

◆ Annex Figure 4.4. ***Phases of an LCA***



Source: ISO 14040, 1997.

ISO is compiling four standards for this field:

- ISO 14040: Environmental management – Life cycle assessment – Principles and framework;
- ISO 14041: Environmental management – Life cycle assessment – Goal and scope definition and inventory analysis;
- ISO 14042: Environmental management – Life cycle assessment – Life cycle impact assessment;
- ISO 14043: Environmental management – Life cycle assessment – Life cycle interpretation.

ISO 14040 was adopted and published 1997. ISO 14041 also acquired the status of an ISO standard in 1997. ISO 14042 has now entered the main stage of development, whereas ISO 14043 is still in the exploratory stage. As far as the standards for ''Life cycle impact assessment'' and ''Life cycle interpretation'' are concerned, a considerable amount of work remains to be done in the sphere of interpretation. Common to all the proposed standards is the relatively large amount of freedom left to those carrying out LCA studies. On the one hand, this reflects the fact that LCA is still in its infancy. On the other, the framework of investigations, as well as their scope and depth of detail, depend to a great extent on the object of the study and its intended use. Thus, a generally valid definition of a standard would not take this heterogeneity sufficiently into account.

Annex 4.3

REVIEW OF LIFE CYCLE ASSESSMENTS

The following review is limited to Germany, Italy, Sweden and Switzerland.[1] It identifies and maps ongoing and completed LCA studies and is based on the following information research methods:

- mailing questionnaires to selected enterprises and institutions;
- contact with researchers, consultants and other key people;
- analysis of IÖW's existing bibliography (Grotz and Rubik, 1996);
- examination of relevant journals and publications;
- use of online databases.

GENERAL APPLICATION

Annex Table 4.5 presents the total results of known LCA studies. In Germany, almost 300 studies have been compiled or are in the planning stages. In Switzerland and Sweden, some 150 studies have been recorded, whereas Italy, by contrast, lags behind.

Annex Table 4.5. **Known LCA studies in various countries**

Studies	Italy	Switzerland	Sweden	Germany
Completed	27	149	137	250
Current	n.a.	n.a.	6	36
Projected	n.a.	n.a.	2	2
Total	27	149	145	288

n.a. = not applicable

It should be emphasised that the statistical data are incomplete, as a number of studies could not be included due to commissioning bodies' requests for confidentiality.[2] The figures should be regarded as a lower limit. An exact statistical analysis poses several serious problems:

- With regard to ongoing LCA studies, the degree of information is sometimes quite meagre. The commissioning body is known, but it is not possible to supply a publication date.
- The commissioning body of some LCA studies is not mentioned in the studies themselves. These studies have been allocated to the category "unknown commissioning body".
- Some businesses contacted returned completed questionnaires, indicating that they had commissioned several LCA studies. If an actual figure was mentioned, this number was counted; if an actual figure was missing (answer "More"), it was counted as "one" LCA study.
- Some enterprises interviewed indicated that they had completed LCA studies and also that LCA studies were under way. In such cases, the study was counted twice, once for the completed LCA study, once for the ongoing study. The ongoing study was not included in the statistical analysis with respect to year of publication, commissioning body, business and subject.

- The statistical information presented below should be viewed in the light of the above reservations. The analysis is classified according to year of publication, commissioning body, business sector(s) involved, size of commissioning enterprise, and products investigated.[3]

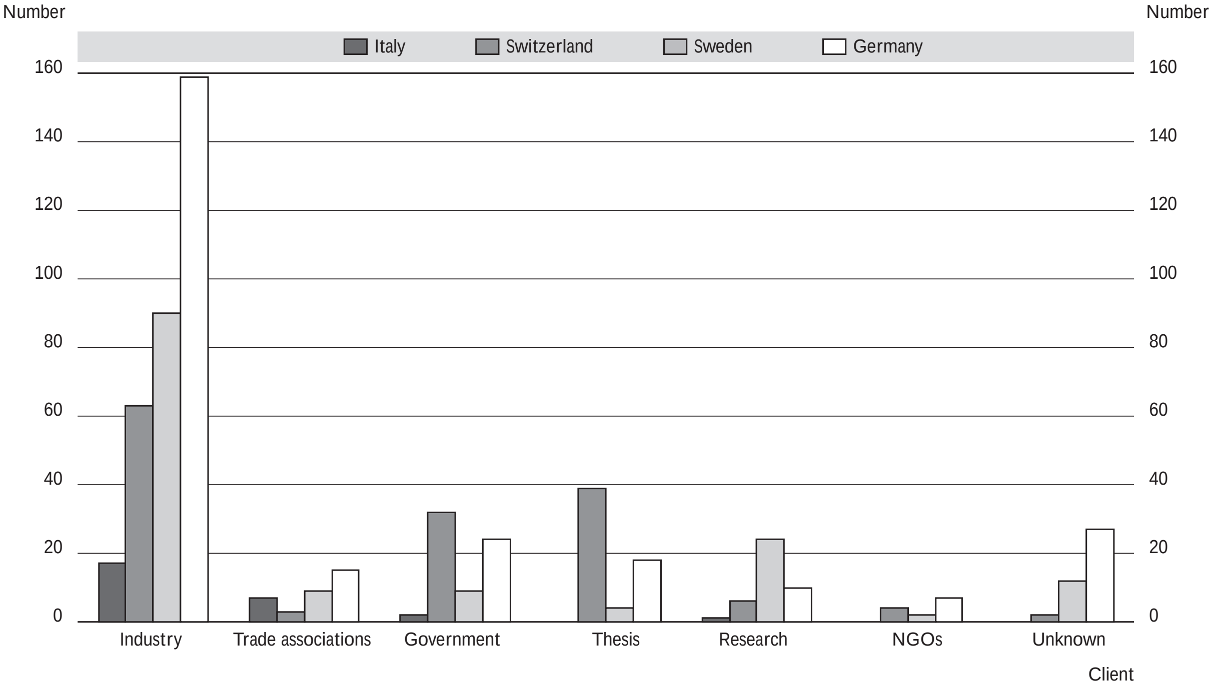
YEAR OF PUBLICATION

Almost no LCA studies were carried out before the beginning of the 1980s, but their numbers increased from the mid-1980s and gained momentum in the 1990s. In Germany, there have been at least 16 studies a year since 1990; the figure of seven studies for 1996 should by no means be interpreted as a downward trend, since at the time of the statistical survey (summer 1996) a considerable number of studies had not been completed. Moreover, there is always a time lag between completion of a study and its public disclosure. In Switzerland the number of LCA studies has stood at 15-20 a year during the present decade; and in Sweden the boom began in about 1992, since when almost the same number of studies has been recorded as for Germany.

COMMISSIONING BODIES AND MOTIVATORS

Annex Figure 4.5 gives a breakdown of commissioners of LCA studies. In Germany, companies commission most LCAs (61 per cent), followed by studies jointly commissioned by trade associations. The public sector is also an important commissioning organisation, although it ranks much lower than the private sector. In Switzerland, LCA studies commissioned by companies are also very significant (42 per cent); compared with Germany, the public sector is also a significant commissioning organisation. In Sweden, the private sector commissions approximately 60 per cent of the studies, and the public sector has a relatively insignificant share. In Italy, the private sector predominates as well.

◆ Annex Figure 4.5. ***LCA commissioning organisations***



Source: Ambiente Italia *et al.*, 1997.

However, the role of the public sector should not be underestimated, as LCA studies commissioned by the public sector have repercussions in the private sector. Whereas LCA studies commissioned by the public sector attach greater importance to generic data and tend to publish ‘‘average’’ numbers, the private sector is more interested in and reacts to specific position rather than to the average. LCA provides a very suitable tool for this.

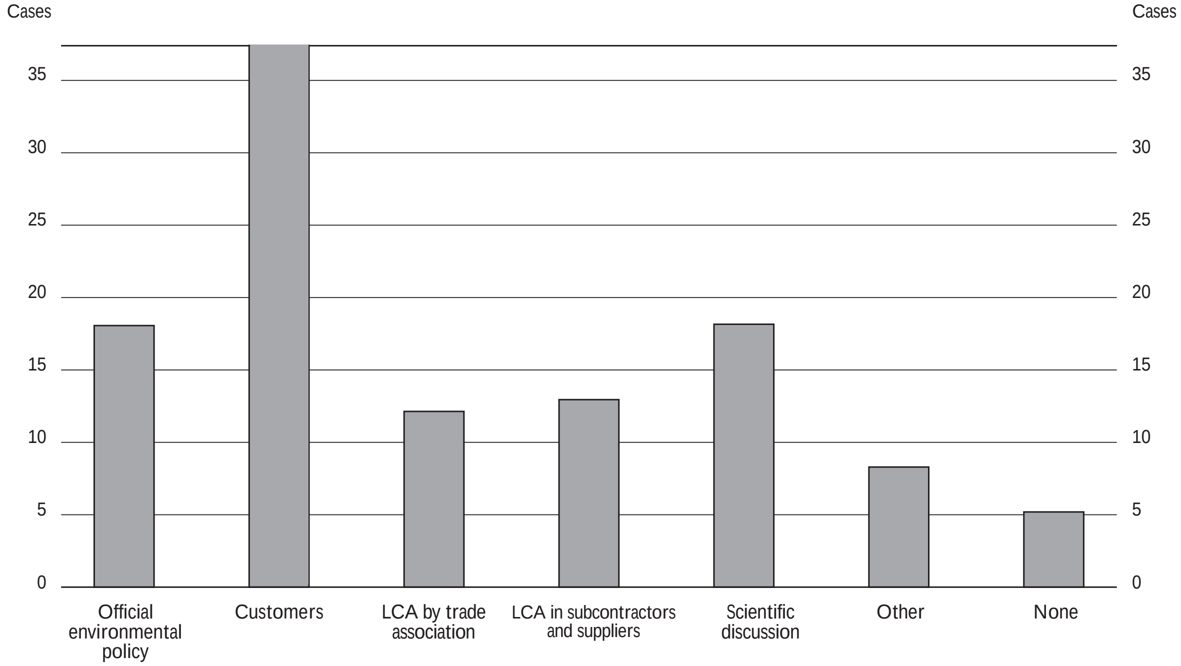
Some instruments of national, product-oriented environmental policy (Oosterhuis *et al.*, 1996; Rubik and Teichert, 1997) refer explicitly or implicitly to LCA or life cycle thinking, as in the case of the German ‘‘blue angel’’ eco-label scheme and the new German waste management act (*Kreislaufwirtschafts- und Abfallgesetz*). Such initiatives stimulate the application of LCA by the private sector; for example, the European eco-label scheme is explicitly based on the results of LCA studies.

In addition to public policy, the market can strongly motivate businesses to adopt LCA. As retailers and consumers demand information on the environmental characteristics of products, some companies use the results of their LCA studies in marketing, and competitors are sometimes forced to react by presenting their own LCA-based information.

Public policy and the market have also stimulated enterprises or a sector (*e.g.* automobile and chemical industries) to carry out joint LCA studies. In-house factors also motivate such studies, *e.g.* initiatives by management or departments with an environmental brief.

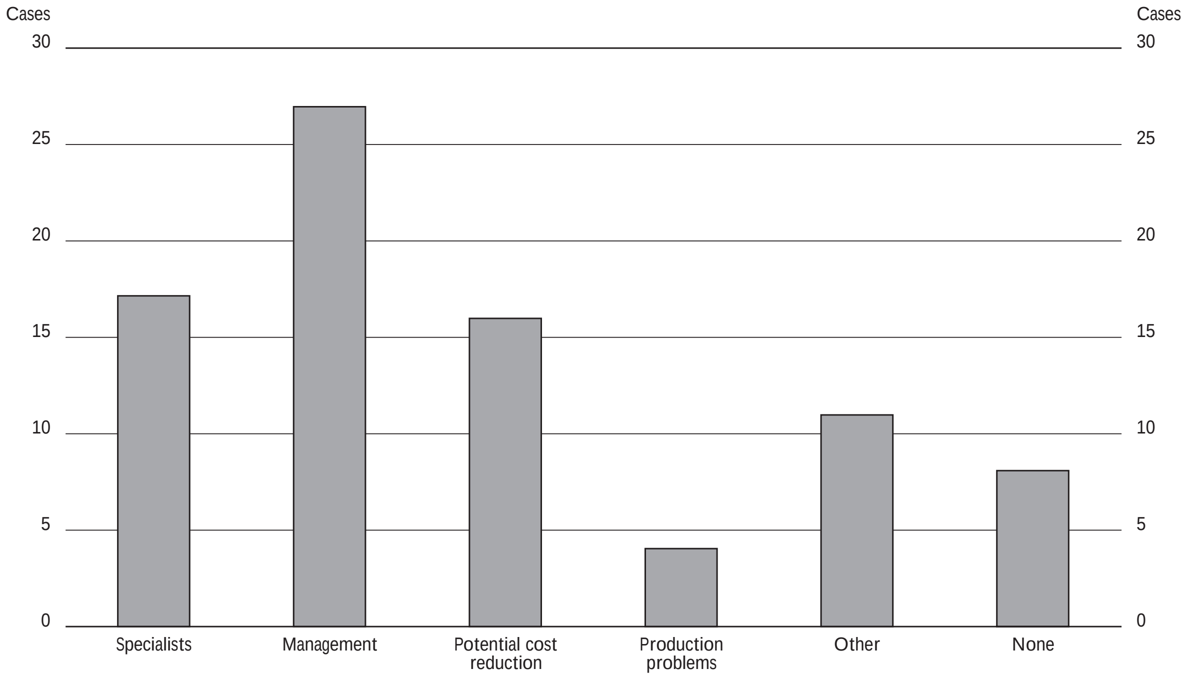
The findings of a survey conducted by IÖW for Germany show that there is almost always a combination of internal and external factors (Annex Figures 4.6 and 4.7). A clear minority of the companies covered by the IÖW survey stated that internal or external influences alone, 9.48 per cent and 15.18 per cent, respectively, played a part in determining their decisions. Reaction to consumers’ increased environmental awareness outranked all other influences. In other words, retailers and consumers are such a powerful market force that their purchasing attitudes can influence producers and

◆ Annex Figure 4.6. ***External influences on German companies to use LCA***
Absolute number of responses



Source: IÖW, 1995.

◆ Annex Figure 4.7. ***Internal influences on German companies to use LCA***
Absolute number of responses



Source: IÖW, 1995.

push them towards an environmentally oriented course. Pro-LCA attitudes were also influenced, to a certain extent, by environmental policy and by scientific discussion. The number of studies made in co-operation with a trade association or with subcontractors and suppliers was relatively insignificant, but those that exist indicate that there is a certain amount of co-operation among companies in terms of LCA.

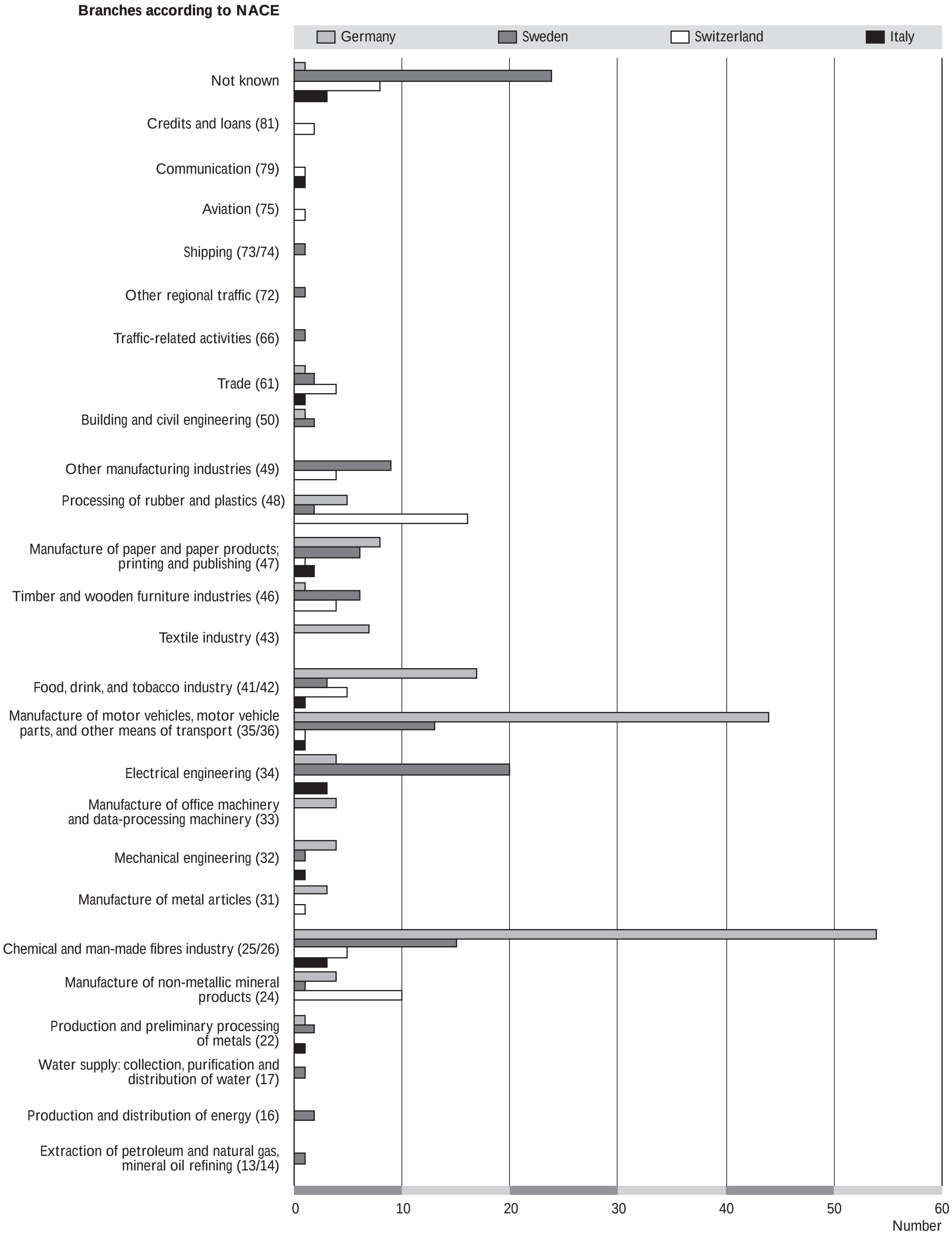
Environmental protection appears chiefly to be the domain of management, since within companies, the impetus to conduct LCA studies has come largely from management (Annex Figure 4.7). The potential for reducing costs, notably in terms of less use of resources, is also not without significance, and many businesses have realised that environmental protection and profitability are not necessarily mutually exclusive. In this context, costs can be reduced above all by saving resources. The fact that problems with a certain product have only rarely provided the motivation for an LCA indicates that general ecological orientation rather than concrete problems is the decisive factor for using this tool.

PARTICIPATION IN LCA BY VARIOUS INDUSTRIES

Annex Figure 4.8 shows that most LCA commissioning bodies are companies; these are classified according to their primary economic activity.

In Germany, the chemical industry and the motor industry are the most important commissioners of LCAs. The food processing and luxury foodstuffs industries are also of consequence. To date, all the other sectors account for less than ten LCAs each. An analysis of companies by size (determined by number of employees) shows that 84 per cent of businesses that compiled or commissioned LCA are large-scale enterprises. Only 16 per cent are small and medium-sized enterprises, *i.e.* with less than 500 employees.

◆ Annex Figure 4.8. ***LCA commissioning bodies in the private sector***
By branch



Source: Ambiente Italia *et al.*, 1997.

In Switzerland, the rubber and plastics processing industry commissions the most LCAs (16 studies), followed by the handling and processing of non-metallic minerals/glass manufacture and processing (ten studies). All other branches account for less than 10 per cent. In Sweden, electrical engineering stands first (20 studies), followed by the chemicals industry (15 studies) and the automotive industry (13 studies). As in Germany, large-scale companies predominate. For Italy, the chemical industry and electrical engineering appear to have the largest share.

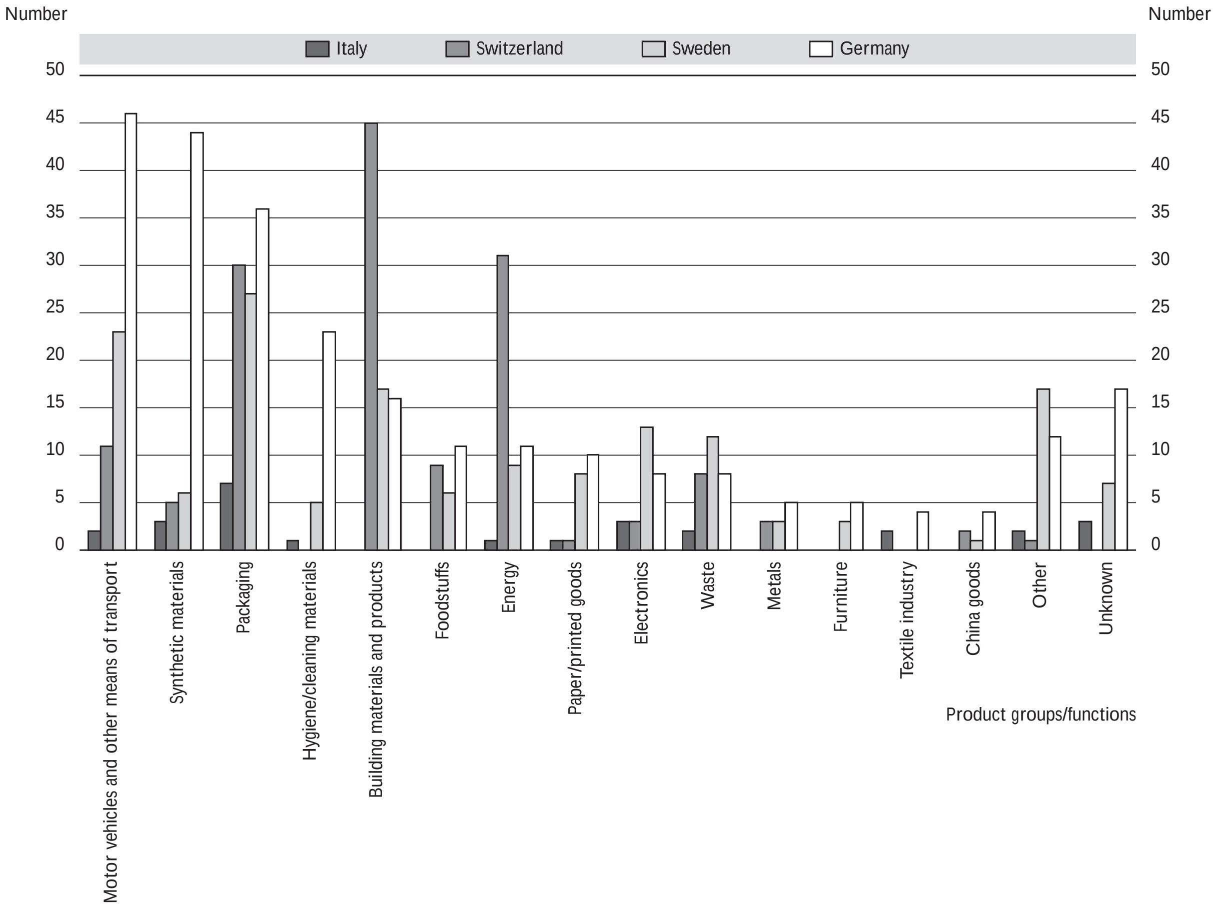
The level of in-house competence and experts is often important. For instance, the multinational Procter & Gamble employs a staff of 15 world-wide, who only work on LCA. Dow Chemical and Volvo each employ six persons in this area (Atlantic Consulting *et al.*, 1996). It is, however, not possible to make a generally valid statement about intensity.

BIOTECHNOLOGIES AND BIOTECHNOLOGICAL PRODUCTS

Compared with commissioning bodies, the product groups covered by LCA studies are quite broadly distributed (Annex Figure 4.9).

In Germany, motor vehicles/motor vehicle components/transport, chemical products, and packaging are similar in importance (between 36 and 46 LCA studies). Other significant product groups are in the areas of hygiene/cleaning and construction materials. In Switzerland, the construction materials

◆ Annex Figure 4.9. ***LCA by product group***



Source: Ambiente Italia *et al.*, 1997.

branch is of paramount importance (45 LCAs), followed by energy and packaging (31 and 30 LCAs, respectively). In Sweden, most LCA studies were compiled in the packaging branch (27 studies), followed by motor vehicles, construction materials, electronics and waste. In Italy, packaging predominated (seven studies).

According to available studies, biotechnology appears to be underrepresented in LCAs. Examples are to be found in the areas of cleansers and detergents, where individual substances (enzymes and tensides) have been investigated by LCA for waste technologies and renewable raw materials. It should be recalled that only studies which have been publicly disclosed are considered here. It is generally assumed that there are many in-house LCA studies whose existence is simply unknown.

NOTES

1. This inventory is based on a joint project, commenced in June 1996, by the Institut für ökologische Wirtschaftsforschung (IÖW) and four other institutes, namely Ambiente Italia (Milan), Gothenburg Research Institute (Gothenburg, Sweden), Institute for Prospective Technological Studies (Seville, Spain), and Oekoscience (Zurich). The title is "The use of LCA in business decision-making processes and its implications for environmental policy". It is supported within the framework of the EU Environment and Climate Programme. Within the scope of this project, comparative statistical data were obtained for Germany, Italy, Sweden, Switzerland.
2. For example, by the end of 1991 the American company Franklin Associates had compiled about 70 studies, of which, however, only four are known. The OECD stated that only 10 per cent of the Franklin studies are available to the public, only 5 per cent of the French consultancy Ecobilan (OECD, 1995). These figures were recently slightly modified; accordingly, 30-60 per cent of all LCA studies commissioned by companies are for internal use only (Atlantic Consulting *et al.,* 1996).
3. Most LCA researchers do not restrict the term "product" to material products, but include processes and services.

Annex 4.4

RESEARCH REQUIREMENTS

GENERAL RESEARCH REQUIREMENTS IN THE FIELD OF LCA METHODOLOGY

The following discussion of research requirements is based on the work of LCANET – Finnveden, 1996; LCANET Board and de Haes, 1996; Wrisberg, 1997*a*.

Clarification of the relationship between LCA and other decision-supporting tools

This annex contains an analysis of the specific features and uses of other analytical decision-supporting tools, discusses when and for what decisions the various tools should be used, and how LCA and other tools can complement each other. Specific issues to be addressed are:

- principles for selecting the most appropriate tool or tools;
- integration and harmonisation of LCA with other approaches, including "green accounting" and other types of goal-setting, EMAS and ISO 14000;
- cross-fertilisation of approaches: are there elements of LCA which can be exploited elsewhere, and *vice versa*?

The development of tools combines the features of "life cycle approach" and "specific process", *e.g.* an environmental impact analysis (EIA) of a whole production chain or system, or a cradle-to-grave risk assessment (RA). New tools may integrate social and economic aspects into LCA methodology, as is the case in the technology assessment (TA) approach (for definitions, see Chapter 4). Life-cycle approaches can be applied to more complex systems involving uncertainties due to prospective changes in technology, product design, consumer expectations, etc., and to dynamic analysis, including stability of material flows and dependence on information and financing.

DEFINITION OF GOAL AND SCOPE: INVENTORY ANALYSIS

The main problems relating to the definition of goal and scope are associated with the (frequently normative) choices that have to be made. What are the arguments behind decisions to disregard impact categories, system boundaries, data quality and assumptions? The reasons may range from application limits, lack of data, need for simplification (indicators), etc. How can the relevant environmental inputs and outputs and the relevant process be determined?

DEVELOPMENT OF AN ITERATIVE APPROACH

In order to establish an iterative approach for LCA, the following areas require further development:

- Screening methods, including "cheap, easy, and quick" techniques that provide less detailed but soundly based findings that still satisfy stakeholder expectations.
- Scope-dependent screening methods. Can a relationship be established between the products and services of a particular economic sector and the elementary (environmental) flows to be considered?
- Inventory analysis geared to actual impact assessment by developing inventory methods to explore the possibilities of the "only above threshold" approach.

SYSTEM BOUNDARIES

The main question is: Which activities and processes are part of the production system and which are part of the environment? Two situations can be distinguished:

- Biological processes, such as forestry, may either be considered as part of the environment or as part of the economic system. When considered as part of the economic system, sunlight, CO_2, H_2O, etc., are environmental inputs, but biomass is the input when biological processes are considered as part of the environment.
- Waste to landfill may be considered part of the economic system (emissions and production of methane as an energy source) and part of the environment (solid waste as output to the environment).

There is need for further research in the following areas:

- Criteria for deciding whether a process is part of the system or part of the environment, especially for biological processes and waste management.
- Simple decision rules for including background processes and cut-off criteria or methods for estimating higher order processes.
- Development of models for systems in which materials are recycled through cascades of use.
- Determination of CO_2 fixation by materials made from renewable resources as a function of product lifetime and of principles to ascertain how CO_2 fixation is related to CO_2 release.
- Easily applicable scenario techniques to incorporate market or technology changes in the inventory analysis. If LCA is to be used to predict future states, how should scenarios be defined? What is the influence of changing technologies and market shares on the outcome of an LCA?

PRINCIPLES FOR DATA SELECTION AND DATA QUALITY

Research geared to the following methodological issues is needed:

- Development of a data quality assessment method.
- Methodological choices, in particular in relation to data concerning generic utilities and commodities, such as electricity, transportation, different types of waste management processes (including landfill, incineration, composting, etc.) and basic materials production (*e.g.* fuels and bulk materials, including those for packaging). The main question is: From which utilities should the data be taken, in which situation, or which averages should be used?
- Criteria for using "foreground" data (*i.e.* specifically related to the product system) and "background" data (*i.e.* basic utilities and commodities).
- Time horizons regarding technology: How long can data be assumed to be representative?
- Regional aspects, *e.g.* with respect to the origin of raw materials.

ALLOCATION PROCEDURES

More detailed studies are needed on allocation and should address the following points:

- Analysis of the significance of allocating to a system level or to a process level, including principles for when to allocate to processes and when to systems.
- Relevance and consistency of allocation principles and development of criteria for using a certain allocation principle.
- Further improvements in quality-based allocation procedures, allocation systems (cut-off, avoidance of primary production, cascade allocation, including dynamic and non-linear modelling), and allocation principles (physical, economic).

LIFE CYCLE IMPACT ASSESSMENT (LCIA)

Framework and methodology of LCIA for different application areas, stakeholders and beneficiaries

It is still an open question whether different applications actually require different LCIA frameworks and methodology. A better understanding of the linkages between methodology and application is therefore an important research area. It is not unreasonable to assume that the requirements for one element (*e.g.* characterisation) may be different if the characterisation is to be used as an input to a specific weighting method, or if it is to be used as the endpoint of the LCIA. There may thus be a need, and a possibility, for endpoint-dependent methodologies and frameworks.

Indication of actual instead of potential environmental impact

A top-down approach may be used, starting with the type of statements that are desired as results, and working backwards through the impact assessment to the inventory analysis in order to understand the type of information required in each phase.

Definition and selection of impact categories

The choice of impact categories is a normative one. The choice should, however, be consistent with the weighting. It is therefore important to develop a better understanding of the relationship between different normative standpoints (as expressed in the weighting), of the general impact categories, and of the choice of impact categories. On the other hand, normative choices can also be made by deleting categories from a single default list. If so, only one default list would be required.

Classification

When allocating material flows to environmental impacts, the following aspects should be investigated:

- assignment of parallel, serial, indirect and combined impacts;
- handling of intermediate materials entering or leaving the system studied.

Characterisation

There is a considerable need for systematic research to develop characterisation methods and factors, which should include aspects such as:

- decision on which dimensions of impact information to include;
- consideration of the cause-effect chain;
- definition of the effect in the cause-effect chain;
- development of a quantitative method;
- calculation of characterisation factors;
- development of characterisation methods, using definitions of effects closely related to the areas for protection;
- development of a quantitative method of characterisation;
- calculation of characterisation factors;
- development of a methodology for all impact categories, taking spatial information into account;
- investigation of the appropriateness and of the implications of taking background information into account;
- investigation of the implications and subsequent development of a modified framework in which fate analysis and effect analysis are split into two elements.

Research activity should be intensified, particularly with regard to the following impact categories:

- development of classification and characterisation for ‘‘land’’, taking different system boundaries and areas for protection into account;
- development of methods for differentiating between the abiotic and biotic stock of resources and assessment of material flows;
- development of methods for acidification and eutrophication, including full fate analysis;
- development of classification and characterisation for toxicological impacts, taking different exposure situations into account;
- development of methods for non-toxicological impacts on human health;
- further development of classification and characterisation of photo-oxidant formation.

Weighting

Since there are ethical and ideological values involved in assessment and since there is unlikely to be a consensus on such values in an open democratic society, it can be expected that several assessment methods and sets of assessment weighting factors will be developed. In order to find out how different groups of people assess different aspects, it may also be useful to use different assessment methods and sets of assessment weighting factors in specific case studies.

It is imperative to evaluate the role of weighting in LCA by:

- developing procedures for weighting, using panel approaches;
- developing monetarised weighting methods, *i.e.* estimating costs for protecting or repairing the environment, soil remediation, or integrated pollution protection systems;
- evaluating the applicability and acceptability of physical single score methods, which are used when it is useful to compare energy, material use, or production within a single process on an MJ or kg basis.

INTERPRETATION

Defining the role of interpretation

The role of interpretation is defined in relation to other aspects of the LCA framework, *e.g.* the weighting, and to external aspects. The improvement assessment aspect has not yet been clarified. The role of interpretation will probably depend on the application, the stakeholders and the beneficiaries of the study, although it is not yet clear how. It may also depend on which steps have been performed previously. It may be different if no impact assessment has been performed, or if the endpoint of the impact assessment is classification or characterisation and a weighting has not been performed.

Development of methods for sensitivity analysis

A sensitivity analysis should include the data in the inventory analysis and all quantitative elements of the impact assessment. Research should consider existing methods, including Monte Carlo simulation, and specifications of the preconditions for carrying out a sensitivity analysis. Different types of statistical distribution should be considered. The results may be further used in different types of statistical analysis to answer questions such as: Is the difference between systems A and B in relation to parameter X statistically significant?

Development of procedures for uncertainty analysis

Procedures for uncertainty analysis should address the following items:

- methodological uncertainties due to choices in the definition and scope and inventory analysis (time, space, allocation, technology, size, marginal/average);

- uncertainties in the classification;
- uncertainties in the characterisation related to methods, models, assumptions;
- uncertainties associated with different approaches to normalisation;
- analysis of uncertainties associated with different weighting methods and geographical boundaries.

Development of methods for dominance analysis

A dominance analysis can result in identification of the most important contributions to the total result.

Development of methods for marginal analysis

A marginal analysis provides information on what overall changes are due to a change in the life cycle. This type of analysis can greatly increase the value of an LCA. By introducing various scenarios (*e.g.* What happens if process A is changed to process B?), a great deal of useful information can be produced which is interesting in connection with an improvement analysis and many other applications of LCA.

DATABASES AND SOFTWARE

Principles and requirements for setting up good databases with appropriate software have to be developed. This means addressing the following needs:

- harmonisation of ongoing activities relating to data format, nomenclature, and exchange of inventory data;
- requirements for the implementation of data quality assessment;
- procedure for updating, including specification of time interval;
- development of software and databases, considering spatial and temporal aspects of flows in relation to impact assessment.

Advanced modelling and database techniques can be used to represent the time and space pattern of environmental inputs and outputs (*e.g.* coupling LCA with geographical information systems).

RESEARCH REQUIREMENTS AT THE LCA/BIOTECHNOLOGY INTERFACE

In principle, there are good reasons for conducting LCAs for biotechnological products and processes. The small number of known LCA studies for biotechnological products and processes is due to the fact that this instrument has been insufficiently developed. There is, however, still room for improvement with regard to developing or adapting this tool to the particular requirements of biotechnology. The following obstacles still need to be overcome:

- Because biotechnological products and processes are often based on renewable resources, question arise concerning the interpretation of renewable resources, the use of agricultural land, and the allocation of CO_2 credits.
- In many cases, the baseline data for biotechnological production are inadequate. Access to vital information is impeded because biotechnology companies are often unwilling to release it on the grounds of confidentiality and company strategy.
- Only in exceptional cases is sufficient information currently available on mass and energy flows.
- Process parameters, such as type and amount of emissions into air, water and soil, are not readily available.
- It is difficult to make generalisations or to apply conclusions from one biotechnological production process to another because the majority of processes to date are "unique".

When a bioprocess is compared with a ‘‘conventional’’ process, many issues arise:

– In addition to technical details, which areas need to be addressed (*e.g.* public opinion)?

– Boundary setting is complicated and is open to discussion.

The advantages of LCA for biotechnological products and processes lie in the possibility of concentrating on those links in the production/consumption chain that are effectively relevant to an environmental comparison, *i.e.* determine environmental differences between the alternatives compared. This provides a chance to optimise the processes under consideration with respect to these points.

With regard to the interpretation of the findings, a general discussion is under way, which means that discussion of the interpretation of an LCA is not exclusive to the field of biotechnology.

Annex 6

POLICIES AND LEGISLATION IN CANADA, JAPAN AND GERMANY

CANADA

In 1993, the federal and provincial governments announced a National Commitment to Pollution Prevention through the Canadian Council of Ministers of the Environment, on the basis that pollution prevention is a key element of the sustainable development policy and will contribute to long-term sustainability by linking environmental protection and economic efficiency. Canada is developing a national strategy for Action on Pollution Prevention. Pollution prevention is essentially the use of processes, practices, materials or energy that avoid or minimise the creation of pollutants and wastes.

It is recognised that methods of implementing pollution prevention will vary among industrial sectors. For the manufacturing sector, they have been described as manufacturing innovations to avoid the use or creation of pollutants through raw material substitution or closed loop processes that recycle within the plant.

The Conference Board of Canada (CBC) indicated that industry drivers for involvement in environmental initiatives are: impending or anticipated regulation, cost savings, efficiency gains or return on investment, and anticipated market share and public image (CBC, 1996).

Canadian policies with respect to toxic chemicals and waste management are moving towards a pollution prevention model that emphasises improving processes to avoid problems rather than a reactive model. This is embodied in government legislation, voluntary programmes and economic incentives. The government manages and regulates toxic substances through all stages of their life cycle.

Authorities across Canada have taken legislative and regulatory action to control the use of toxic substances and their impact on the environment. Under the Canadian Environmental Protection Act (CEPA), toxic substances are managed at each stage of their life cycle to achieve specific end points. Certain specified toxic substances have been identified as priority substances for environmental and health assessment and potentially for regulation. The second aspect of the legislation under the Canadian Environmental Protection Act is a requirement for all "new" substances, *i.e.* those not on a list of domestic substances, to be notified and assessed for environmental and human safety prior to import or manufacture in Canada, including any "new" substances produced through biotechnology.

Also under CEPA, there is a legal basis for a national pollutant release inventory, which requires companies that meet certain criteria to collect and submit to the government information on releases to air, land or water of specified substances.

Energy

Canadians use more energy per person than people in most other industrialised countries owing to its cold climate, energy-intensive industrial base (*e.g.* pulp and paper, iron and steel production and mining) large land area, and low population density, which creates high demand for transportation services and relatively low energy services. Many aspects of energy production and use, from exploration to final consumption, may affect human health and the environment. Correspondingly, a number of federal government initiatives have evolved, largely of a voluntary nature, which are oriented towards:

- reduced vehicular traffic;
- greater conservation measures;
- improved environmental quality;
- improved economic efficiency of resources;
- enhanced quality of life.

These initiatives are based on programmes and suggested changes to transportation infrastructure, demand management, traffic management; cleaner technologies, education and outreach, transit management, and urban structure and design.

Air

In regard to the reduction of releases into the air, Canada signed in 1987 the Montreal Protocol and undertook a control programme to protect the ozone layer. Under the Montreal protocol, the primary target is the phase-out of ozone depleting substances (ODSs). The present timetable calls for elimination of non-recoverable uses of HCFCs (hydrochlorofluorocarbons) by 2010, the elimination of HCFC-22 in new equipment by 2010, as well as a 25 per cent reduction in the consumption of methyl bromide by 1998 and complete elimination by 2010. The control of ODSs is subject to the Ozone Depleting Substances Regulation of CEPA. A second regulation on the ozone-depleting substances products covers the control of manufactured products containing ODSs, such as aerosols and plastic foam food packaging. There are also codes of practice for the elimination of fluorocarbon emissions from refrigeration and air conditioning systems and for the halons.

There are also risk reduction programmes committed to a 50 per cent reduction in sulphur dioxide emissions and to capping emissions related to acid rain in eastern Canada.

Toxic substances

In 1994, the federal government released a new policy to provide direction for all federal initiatives dealing with toxic substances. The Toxic Substances Management Policy is based on the principles of sustainable development and pollution prevention, with the emphasis on the need for preventive action and use of precautionary approaches to the management of toxic substances. The Chlorine Action Plan, which focuses on the virtual elimination of harmful chlorinated substances, is part of this policy.

Federal Toxic Substances Management Policy (TSMP)

For the most hazardous substances, the management objective is virtual elimination from the environment; while for others, the objective is management throughout the substance's life cycle to prevent or minimise release into the environment. Domestic actions are co-ordinated primarily through Environment Canada's Strategic Options Process which seeks to identify management options based on stakeholder participation and also allows for co-operation with the provinces in identifying priorities and management approaches. While the preferred management approach is pollution prevention, the policy recognises the need for:

- action to deal effectively with entry from domestic sources;
- international action to deal with entry from foreign sources through long-range atmospheric transport;
- remediation to deal with substance already present in the Canadian environment.

Under TSMP, 13 substances have been identified as candidates for virtual elimination because they have been characterised as persistent, bioaccumulative and toxic. All are highly chlorinated. It is the government's policy to make those who generate or use these substances responsible for ensuring that releases are below the level of quantification and for developing management plans to eliminate emissions of such substances based on an analysis of risks, costs and benefits.

Chlorinated Substance Action Plan

Established in 1994, the Chlorinated Substances Action Plan, under the Toxic Substances Management Policy calls for complete life cycle management of all substances of concern that are released into the environment. Many chlorine-containing substances fall into this category. The Action Plan calls for targeting critical uses and products and eliminating the most harmful chlorinated substances, taking a sectoral approach to the management of chlorinated substances and entering into environmental performance agreements with key industrial sectors.

Under the Action Plan, nine chlorinated substances have been targeted for significant reduction under ARET, with reduction of 98 per cent from the base year 1988 by 1995, and 99 per cent reduction by 2000. Emissions of another 24 chlorinated substances with total emissions of in excess of 3.26 million kilograms in the base year were reduced by 67 per cent in 1995 and are projected to be reduced by 81 per cent by 2000. Specific industries involved in the ARET programme through memoranda of understanding (MOU) with the government are the automotive industry, the automotive parts industry, the dry cleaning sector, the polyvinyl chloride sector, the printing and graphics sector, and industries using chloranil dyes and pigments.

Waste

Most provincial governments have established a legislative basis for reducing the generation of hazardous waste. Different provincial government plans target different waste streams. British Columbia has initiated action on ways to make plastic substances more recyclable and to reduce their presence in the waste stream, Quebec has developed a new code of practice in solid waste landfill and gas management under the Climate Change Convention which aims to reduce methane emissions.

The North American Agreement on Environmental Co-operation (NAAEC) under the North American Free Trade Agreement (NAFTA) is a trilateral initiative to integrate developmental and environmental concerns and came into effect in January 1994.

The distribution of responsibility for sustainable development within Canada is complex. While the federal government conducts international treaty negotiations on behalf of Canada, responsibility for environmental and sustainable development falls within the legislative jurisdiction of both federal and provincial levels of government.

The positive effect of government regulations and policy

The federal pollution prevention strategy (Pollution Prevention: A Strategy for Action) encourages firms to move away from end-of-pipe solutions and towards anticipating and preventing environmental damage. This has resulted in new processes, technologies and products that reduce environmental stresses.

Cleaner processes and products mean processes and products that consume less energy and material resources, generate less pollution or waste, or use renewable resources rather than petroleum- or coal-based feedstocks as feed. There are many reasons why an operator would switch to a cleaner process or product. Some of the more important factors most often mentioned are:

- availability of raw materials;
- cost factors;
- market demands;
- safety and health considerations;
- environmental considerations;
- product liability;
- public image.

While the above factors are not given in any particular order, it is clear that environmental considerations are only one of many aspects in the move to new products or processes. Product changes are more frequent (well-known examples include the phasing out under the Montreal Protocol of ODSs such as CFCs, carbon tetrachloride, and methyl chloroform and the use of vegetable-oil-based printing inks; process changes are rarer and in most cases also involve some product change. Moreover, the actual reasons vary from case to case, as the following case studies, primarily on process changes, serve to demonstrate:

– introduction of the dimensional stable electrode in the production of chlor-alkali;

– phase-out of the mercury cell for chlor-alkali production;

– use of chlorine dioxide rather than elemental chlorine in the bleaching of pulp and paper;

– use of aqueous cleaning systems to replace chlorinated hydrocarbon solvents;

– use of the fermentation process instead of the petrochemical route to produce ethanol.

Case studies

The introduction of the dimensional stable electrode in the production of chlor-alkali

In the past, the use of the graphite electrode in the production of clor-alkali led to the formation of a number of undesirable by-products, such as octachlorostyrene and hexachlorobenzene. Since the introduction of the dimensional stable or metal electrode, the formation of these by-products has virtually been eliminated.

Operators shifted to these new electrodes not as the direct result of specific government action, either regulatory or other, but rather owing to combination of most of the factors mentioned, the most important of which appears to be economic. The longer service life of the dimensional stable electrode led to significant cost savings.

The phase-out of the mercury cell for chlor-alkali production

This very important process change is clearly a direct result of regulations issued in the 1970s under the Fisheries Act to reduce the amount of mercury discharged into lakes and rivers. Later regulations under CEPA controlled the amount of mercury emitted into the air. Many of the older mercury cell plants were shut down and replaced by membrane or diaphragm cell plants.

At present, only one small plant in Canada uses the mercury cell process. Canada is far ahead of the United States and particularly Europe, where almost half of all chlor-alkali plants still use the mercury cell process. This example clearly shows that strong environmental regulation can lead to the promotion of cleaner processes.

The use of chlorine dioxide rather than elemental chlorine in the bleaching of pulp and paper

Revised regulations under the Fisheries Act and new regulations under CEPA are often cited as the reason for the phasing out of elemental chlorine for bleaching pulp in favour of chlorine dioxide and, to a lesser extent, hydrogen peroxide, to prevent the formation of dioxins and furans in measurable quantities.

However, at least two other factors were instrumental in the Canadian Pulp and Paper industry's decision to invest billions of dollars in moving to new bleaching processes. First, many US customers insist on dioxin- and furan-free pulp, so that they can claim that the products they market are truly dioxin- and furan-free. Second, the German market is insisting more and more on totally chlorine-free paper products, and the world market is increasingly insisting products at least free of elemental chlorine in order to support sustainable development.

The use of aqueous cleaning systems to replace the use of chlorinated hydrocarbon solvents

The introduction in recent years of mainly aqueous cleaning processes to replace solvent degreasers that use chlorinated hydrocarbons is largely the result of voluntary action on the part of industry. The automotive industry has shown environmental leadership, through a Memorandum of Understanding (MOU) between the Motor Vehicle Manufacturers Association and the Ontario and federal governments.

Although the principal chlorinated solvents in use, trichloroethylene and tetrachloroethylene, were declared toxic under CEPA, there are no legal restriction on their use in Canada. The Canadian aeronautical industry, which feels that chlorinated solvents are crucial for their applications, is still a relatively large user. However, under the Strategic Options Process, significant reductions in the use of chlorinated solvents for degreasing were negotiated with industry.

The use of the fermentation process instead of the petrochemical process for producing ethanol

The National Biomass Ethanol Programme is designed to increase the use of ethanol generated through fermentation of biomass to replace conventional petroleum-based fuel for energy applications. This process change clearly meets the definition of a clean process. It is also the direct result of government policy to promote the use of renewable resources. It is not clear, however, whether this policy is inspired by environmental considerations or by the desire to create new markets for existing agricultural products. The cost of producing ethanol in this way is double that of producing equivalent petrochemical products.

Whatever the reason, the recent announcement of the establishment of a new plant in Alberta to produce methyl tertiary butyl ether from barley and butane is further proof that government policy very effectively causes process changes. This gasoline additive is already produced in Alberta from petrochemical feedstock.

Industry perspective

Industry correctly points out that there are many driving forces besides government action which lead to cleaner industrial products and processes. Specifically, many industry initiatives have been taken in response to general public awareness of environmental issues rather than specific government actions. These initiatives have developed through the effect of ENGOs and the media. Therefore, a combination of public awareness and the possibility of legislative action leads to the establishment of progressive industry policies in the environmental area. A typical example of economic incentives in the right social environment is responsible waste disposal. The sheer cost of responsible waste disposal has created a large economic incentive for waste reduction. In Canada, municipal and provincial governments, which have responsibility for waste disposal, played a large part in establishing the economic climate that led to waste reduction measures.

Legislation will drive the development of clean industrial products and processes when the development or adoption of a new product or process is too costly for any one company to take the lead. Where all industrial competitors are obliged to adopt the same measure, as was the case for the replacement of CFCs with HCFCs as blowing agents for insulation foam, the legislation provides for equal competitive industrial strategy.

Other examples of industry initiatives include the fabrication of products such as masking tapes without the use of organic solvents.

Voluntary initiatives

Voluntary environmental initiatives have become increasingly prevalent in Canada over the past several years and take many forms, including covenants between industry sectors, non-governmental organisations, and government. The rationale for these actions is the perception that traditional regulatory, *i.e.* legislative, approaches may not always be the most appropriate method for achieving the desired goals. The motivators or drivers for these voluntary initiatives, as identified by the Conference Board of Canada, are:

– impending or anticipated regulation;

– cost savings or efficiency gains (near term);

– market share and public image (long term).

In most cases voluntary initiatives are regarded as complementary to regulation, with a variety of interplay between the two. One concern with voluntary initiatives is reaching small and medium-sized enterprises, an issue that is primarily being addressed through provincial government programmes.

ARET

Voluntary initiatives have also been taken by industry in support of legislative protocols; the accelerated reduction and elimination of toxics (ARET) initiative is a government-industry joint initiative committed to reducing or eliminating emissions of some 100 substances through voluntary action. A centrepiece of this initiative is the elimination or phase-out of bioaccumulative or persistent toxic substances.

Launched in 1994, the programme has grown to include 278 facilities from eight major industrial sectors representing over 40 per cent of Canada's total industrial production. The programme's short-term goal is to reduce persistent, bioaccumulative and toxic emissions by 90 per cent and all other listed toxic substances by 50 per cent by the year 2000 from 1988 levels. The ARET list includes 117 toxic substances.

JAPAN

Japan has established a national scheme with legislation dealing with the issues of effects on the environment in the broadest sense. At the top of the hierarchy is the Basic Environmental Law, which has been amended over time to accommodate changing national and international views on protection and conservation of the environment and the increasing integration of environmental issues into other areas. The Basic Environmental Law, as amended to reflect the objectives of Agenda 21 arising from the United Nations Conference on Environment and Development (UNCED), is further elaborated in two policy documents: the National Action Plan for Agenda 21 and the Basic Environment Plan.

Moving from overall objectives to specific aspects of environment or health protection, there is legislation that details objectives relevant to each aspect: the Air Pollution Prevention Law, the Water Pollution Prevention Law, and the Law for Punishment of Crimes Relating to Environmental Pollution Pertaining to Human Health.

At this second level, there are more specific laws relating to individual aspects of industry or society, such as the law concerning the examination and regulation of manufacture, etc., of chemical substances (Chemical Substances Control Law) and the Agricultural Chemicals Regulation Law.

Japanese policy clearly identifies lifestyle as a causative agent in pollution and environmental degradation. It addresses change in lifestyle as a central policy issue for achieving the goals of Agenda 21, in particular in the Action Programme to Arrest Global Warming. In the part of the Action Programme, developed in 1991 for the period 1991-2001, which addresses low CO_2 emissions, five items on lifestyle are: the development of recyclable materials and products, excessive packaging and distribution, development and propagation of products with low CO_2 emissions, daylight saving and efficient energy use. In the policy document, Basic Environmental Plan (1993), public participation at all levels of society is a key feature. The document states that wasteful lifestyles must be reviewed and values and conduct must change. It also states that each sector must voluntarily and actively participate in efforts to use the environment wisely and to reduce the burden on it.

Japan established a Basic Environmental Law in 1967, and has amended it several times, most recently in 1993. Article 1 of the law defines the purpose of the basic environmental law as follows: "The purpose of this law is to comprehensively and systematically promote policies for environmental conservation and accordingly to contribute to ensuring healthy and cultured living of this and future generations of the nation and contribute to the welfare of mankind by establishing basic principles as well as to clarify responsibilities of the State, local public entities, enterprises and people with regard to environmental conservation and prescribing the basic matters of policies for environmental conservation.''

As amended in 1993, the Basic Law is intended to implement, at national level, the goals of UNCED. Frequent reference is made to the elements addressed in Agenda 21, including global warming, ozone depletion, marine pollution and decrease in biodiversity. Article 4 refers to sustainable development and reduced environmental burden. In accordance with Article 15, the Japanese government published in 1994 a Basic Environmental Plan. This plan is an expanded policy document which identifies policies relevant to achieving four long-term objectives.

– to build a socio-economic system which fosters environmentally sound materials cycles and minimises environmental load due to human activities;

– to secure a harmonious existence between mankind and diverse wildlife and natural environments;

– to secure participation of all members of society in environmental conservation activities (the Japanese term translated as environmental conservation includes both protection and improvement of the environment);

– to enhance international activities.

The Basic Environment Plan sets the basic concepts and long-term objectives of environmental policy through the 21st century.

Under the Action Plan for Agenda 21, Japan identifies specific goals which have an impact on industrial processes and products. These are indicated under various headings, including protecting and promoting human health, subsections on Urban Health and Environmental pollutants and hazards.

Energy

A continuing theme in the Action Plan for Agenda 21 is the concept of sustainable energy. The plan describes energy as ''an intermediate between environmental conservation and economic growth'' and suggests that to attain the objective of sustainable development there is a need for fundamental reform of the demand and supply structure for energy.

In addressing energy, Japan has introduced several laws regarding the reduction of environmental load as a consequence of energy generation, dissemination and utilisation. The most far-reaching of these are amendments to the law concerning the promotion of the development and introduction of alternative energy.

The Action Plan calls for the integration of environment and development in decision making and makes legal provision for this system. The system was established in 1993 under the Basic Environmental Law, which, in addition to establishing basic principles, contains provisions for formulating the Basic Environment Plan, environmental quality standards, regulatory measures and economic measures.

Under the Basic Environment Plan, there are specific objectives relating to protection of the atmosphere, to protection of the quality and supply of freshwater resources, to environmentally sound management of toxic chemicals and to environmentally sound management of both hazardous and solid wastes.

Air

In terms of protection of the atmosphere, the policy under the national Plan for Agenda 21 is that Japan will move towards stabilising emissions of greenhouse gases through an Action Programme (policy) to arrest global warming (October 1990), and, in January 1993, Japan signed the UN Framework Convention on Climate Change under which it will aim to stabilise carbon dioxide emissions on a per capita basis at the 1990 level and stabilise total emissions at the 1990 level by the year 2000. The target for methane emissions is set at the 1990 level.

Energy supply, industrial production structure, and lifestyle are identified as elements for action. The Action Plan also characterises the development of innovative technologies as a functional approach to stabilising or reducing CO_2 emissions, specifically in the energy production sector and in the area of CO_2 fixation. The 1990 Action Programme identifies the manufacturing, agricultural, forestry, fisheries, construction sectors as the primary targets for implementation of the Action Programme and identifies the introduction of energy sources with low or zero CO_2 emissions.

To achieve the objectives under energy development and efficiency in sustainable development, Japan has established several laws. With regard to industrial development and energy use, Japan identifies a programme of voluntary action to reduce energy consumption. Laws to regulate the emission of sulphur dioxides and nitrogen oxides have been enacted under the Pollution Control Law. Also under this activity are initiatives to promote energy conservation through recycling. A secondary activity is the accession to the Vienna Convention for the protection of the Ozone Layer and the Montreal Protocol on substances that diminish the ozone layer. In 1989, Japan established the Law Concerning the Protection of the Ozone Layer through the Control of Specified Substances and other measures.

Water

A further major initiative under Agenda 21 is the protection of the quality of the water supply through protection of water resources and conservation of the water supply. Identified in this strategy is the effective and rational use of sewage and industrial drainage. Standards for maintaining desirable water quality are ensconced in the Basic Environmental Law and in the Water Pollution Control Law through effluent standards and the application of effluent control measures through appropriate treatment of wastewater from both urban and industrial sources.

In addressing water quality for agriculture and rural areas the Agricultural Chemicals Regulation Law establishes standards for withholding registration of agricultural chemicals on the basis of their potential to pollute water. This initiative also extends to activities involving fertilisers and the development of fertilisers which are not prone to run-off. The policy also identifies initiatives for developing technology initiatives to purify water using the natural water purification functions of ecosystems.

Toxic substances

Policy on toxic chemicals includes expanding and accelerating the assessment of chemical risks through a variety of initiatives. One initiative in this programme is the OECD action plan for evaluating high production/volume chemicals (HPV) (1 000 tonnes or more manufactured in one country). The IFCS (Intergovernmental Forum on Chemical Safety) also calls for the assessment of 500 HPV chemicals by the year 2000.

The Chemical Substances Control Law, established in 1973, was amended in 1986. Under this law, any substance new to Japan, either through importation or manufacture, must be notified to the competent authority and examined with regard to its biodegradation, bioaccumulation, and chronic toxicity. In 1996, there were 320 notifications under the New Chemical Substances provisions of the law. Substances imported or manufactured in quantities of less than one tonne a year require another type of notification. More than 8 000 substances were notified in 1996.

Also under the Chemical Substances Control Law, existing chemical substances are reviewed for the properties of biodegradation, bioaccumulation, and chronic toxicity to establish if they should be classified as Class I specified substances, Class II specified substances or designated substances. Class I substances are poorly biodegraded, have high bioaccumulation potential, and are chronically toxic. Class II substances are poorly biodegraded and are chronically toxic but do not bioaccumulate. Designated substances are poorly biodegraded, do not bioaccumulate, but raise a suspicion of chronic toxicity. By November 1996, 1 087 existing chemical substances were reviewed, nine were designated as Class 1, 23 as Class II and 13 as designated substances.

Waste

Waste management has been under legislation in Japan since 1970 under the Waste Management and Public Cleansing Law (Waste Management Law). The law was amended in 1992 to include measures to restrict waste generation and to promote appropriate waste sorting and recycling. Measures under the amendments include the promotion of waste reduction, planned disposal of waste, including authority to require waste management plans for facilities in municipalities which generate large amounts of municipal solid waste (MSW), regulations on waste handling and treatment, designation of specifically controlled wastes, and designated wastes. Examples of designated wastes include rubber tires, television sets, refrigerators and spring mattresses.

The Law to Promote the Utilisation of Recyclable Resources (the Recycling Law, April 1991), which came into effect in October 1991, establishes a legal framework to promote recycling and designates specific industries that must increase their use of recyclable material, designated categories of products that must contain increasing content of recyclable materials, product categories that must indicate their contents in order to facilitate recycling, and a category of by-products that must be either partially or completely recycled.

The Recycling Law provides authority for several ministries and agencies to establish sectoral basic policies to promote recyclable resources and procedures. The designated industries are paper manufacturing, glass container manufacturing, and construction. Designated product types for recycling which must use Life Cycle Assessment to define the materials for recycling are automobile manufacture and repair, large household appliances, and 16 specific product items, such as tools which use batteries. Products that must be labelled to facilitate recycling include most container types, such as PET bottles and cans, and batteries. An example of a specified by-product subject to recycling under the law is steel slag from the steel industry.

A parallel law, the Law on Temporary Measures to Promote Business Activities for the Rational Use of Energy and the Reutilisation of Recycled Resources, is essentially an economic incentive law coupled to an aggressive action policy addressing three elements of waste reduction – promotion of energy conservation, promotion of recycling, promotion of rationalised usage of designated freon gas – under the umbrella policy of promotion of the rational and appropriate use of resource energy.

Voluntary initiatives

Japanese industry also implemented voluntary action in April 1995 with the establishment of a responsible care programme targeted to achieving the objectives of sustainable development under Agenda 21. The programme aims at "continual improvement and development to ensure that present methods of chemical management are better than those of the past" through "a set of activities aimed at protecting the environment and ensuring safety at all stages of chemical substance life cycles".

As of December 1997, there were 90 member companies in the responsible care programme; they accounted for more than 70 per cent of the value of shipments of the Japanese chemical industry. Under responsible care, specific targets are set. In the area of preserving environmental safety during manufacture and handling there are targets to reduce SO_x and NO_x emissions, energy and resource savings, increase recycle rate and reduce waste. For example, the recycle rate is targeted to increase from 31 per cent, the rate in 1995, to 46 per cent by 2010. In another example, the volume of waste finally landfilled is to be reduced by 40 per cent by 2010, as compared to the 1990 level.

As part of responsible care the member industries have selected 300 substances for a survey of emissions. The substances were selected as the chemicals that may have adverse effects on human health, based on several surveys conducted by local government bodies, the Environment Agency, and US chemical manufacturers. The results of this survey would identify more clearly the routes of entry of the substances into the environment and could serve as indicators for measuring the effectiveness of their activities to reduce emissions and the effects of these chemicals on human health and the environment. The member companies have also set a three-year programme to reduce atmospheric emissions of 12 harmful chemicals, including dichloromethane, benzene, vinyl chloride monomer, acrylonitrile, and dichloroethane. This programme aims to reduce the emissions of each chemical by 20-30 per cent by 1999, as compared with the 1995 level. Member companies had already achieved 34 per cent reduction of the emissions for the 12 chemicals by 1996.

GERMANY

In September 1994, environmental protection was raised to the level of a "state goal" under Germany's Basic Law. Article 20a of the revised Basic Law requires the state, through the legislative branch, to protect the natural basis for life. This forms the foundation for Germany's environmental policy framework and the basis for the German approach to protecting the environment based on protecting life, which includes clean water, air and soil.

In general, Germany's environmental policy framework is based on the belief that environmental protection is imperative for sustaining life on Earth and that the benefits derived from high environmental standards also include job creation and economic benefits. The result has been the establishment of an industry sector consisting primarily of small and medium-sized companies which employ 1.9 per cent of all German workers. The environmental policy covers three general levels of activity:

- continuous development of preventive environmental protection policy;
- environmental remediation;
- involvement in international environmental protection activities.

The objective of these activities within Germany's environmental policy is to safeguard the environment by:

- reducing and remediating existing environmental damage;
- preventing harmful effects on humans and the environment;
- minimising risks for humans, animals, plants and the natural environment (soil, water, air);
- protecting areas of biological diversity.

These objectives are intended to be horizontally integrated into the functions and activities of all government departments and be based on the precautionary principle, the polluter-pays principle, and the principle of co-operation. The result is a series of framework laws with numerous subsidiary laws addressing specific environmental concerns. Water protection is addressed by the framework Federal Water Act and variety of specific legislative measures, including the Wastewater Charges Act, the Washing and Cleansing Agents Act, the Drinking Water Ordinance, and the Ocean Dumping Act.

Overall, the objective of the federal government's environmental policy is to protect the environment by uniting both ecological and economic forces into an ecologically committed social market economy. To achieve this balance, environmental considerations need to be accounted for and anticipatory measures integrated into all economic decisions.

Germany's strategy to attain this overall objective is constant improvement of administrative laws, the creation of economic incentives to encourage more sustainable use of resources, and increased research and development into more innovative products and methods of production.

The main instruments used to implement German environmental policy objectives are largely regulatory instruments (requirements and prohibitions, environmental impact assessments); economic instruments aimed at internalising external costs; and supporting measures that take into account voluntary commitments, funding for environmental or "clean" technologies, and environmental research. In addition, the above instruments are supplemented by provisions relating to penalties and administrative fines with the view that by imposing control charges on emissions and taking ecological aspects more into consideration when determining taxes, important economic incentives to reduce environmental pollution are created (*e.g.* a wastewater charge is imposed on polluters, according to the quantity and toxicity of the wastewater discharge).

As a member of the European Union, German law must also reflect certain legal requirements set out by the European Council. Among these are three directives adopted in 1990 that together formed the basis of Germany's biotechnology and genetic engineering legislation:

- Directive 90/219/EEC Contained Use of Genetically Modified Micro-organisms.
- Directive 90/220/EEC Deliberate Release into the Environment of Genetically Modified Organisms.
- Directive 90/679/EEC Protection of Workers from Risks Related to Exposure to Biological Agents at Work.

Directives 90/219/EEC and 90/220/EEC were implemented into German legislation by the Genetic Engineering Law in 1990. The first version of this law was heavily criticised by industry and academic research owing to bureaucratic burdens that significantly inhibited biotechnology research and investment. The law was amended in 1993 and is generally designed to protect human health and the environment from potential risks associated with products of genetic engineering. Protection under the law is achieved by a classification system which places recombinant organisms into one of four biosafety levels and sets out criteria ranging from construction of containment facilities to handling procedures and record keeping.

Air

The framework legal instrument for air quality control is the Federal Emission Control Act which includes regulations on:

- Plants: This includes power plants, industrial plants (including incinerators), households and small consumers. The objectives are to control emissions of air pollutants (particulate, sulphur dioxide, nitrogen oxides), increase efficiency of heating systems and building insulation to reduce energy consumption for heating by 30 per cent.
- Traffic: since 1985, low-emission vehicles have received tax breaks; since 1993, all new motor vehicles must be equipped with a closed loop, three-way catalytic converter, and all vehicles are subject to a mandatory exhaust gas test. The target for total average fuel consumption is 5 litres per 100 km by the year 2005. Tax breaks for lead-free petrol have led to 90 per cent of vehicles using this fuel. Reduction of sulphur in diesel fuel has led to a 60 per cent reduction in sulphur dioxide emissions from diesel vehicle (as part of the 1985 Helsinki Protocol, Germany agreed to reduce before the year 2000 its sulphur dioxide emissions by 83 per cent compared with the 1980 benchmark level).

For control of low-altitude ozone, a number of measures have been initiated:

- containment of hydrocarbon vapours during fuelling of vehicles (1996);
- nitrogen oxide emission standards for vehicles were made 50 per cent more stringent (under the 1988 Sofia Protocol, Germany agreed to reduce by 1998 its annual nitrogen oxide emissions by 30 per cent compared to the 1986 benchmark levels);
- prohibitions on driving when low-altitude ozone levels exceed a threshold;
- emission-oriented motor vehicle tax aimed at early introduction of low-emissions trucks;
- reduction of solvent emissions from paints and varnishes as well as from industrial operations (under the 1991 VOC Protocol, Germany agreed to reduce by 30 per cent emissions of volatile organic compounds by 1999).

With respect to greenhouse gases, the Federal Republic of Germany is a party to the UN Framework Convention on Climate Change. Germany accounts for about 4.5 per cent (*i.e.* 900 million tonnes) of global carbon dioxide emissions. The goal is to reduce, by the year 2005, Germany's carbon dioxide emissions by 25-30 per cent relative to the 1990 benchmark levels.

To achieve this target measures have been initiated to:

- conserve and economise overall levels of energy use;
- switch to more environmentally compatible energy sources than those in use;
- increase the proportion of energy from renewable sources.

For protecting the high-altitude ozone layer, the federal government supports internationally agreed measures based on the Montreal Protocol. The agreed targets are phase-out of CFCs by 1996, halons by 1994, and HCFCs over the period 2003-2030.

Water

The main focus of the federal government's initiatives for protecting water is the implementation of preventive measures designed to limit or avoid emissions at the source. This shifts the focus from "end-of-pipe" technology to environmentally compatible production and to avoidance and treatment at point of origin. Process engineering measures for avoidance at point of origin of the wastewater and wastewater pre-treatment take priority over later treatment in wastewater treatment plants. Primarily, the instruments within the current federal government framework of water legislation are, whenever possible, directed towards the source of the pollution. Germany's water protection policy provides for protection of surface waters, coastal waters and seas, and groundwater.

Statutory instruments for protection of waters

The federal government is responsible for the adoption of framework laws in the field of water management. The federal *Länder* (states) complete this framework with their own laws, which also provide the necessary procedural and organisational regulations. At the same time, they are responsible for monitoring adherence to regulatory provisions.

The Federal Water Act is the framework water law. It sets the basic regulations on measures for quantitative and qualitative water management. The most important instruments under the administrative laws are compulsory licenses for water use. In addition, it stipulates minimum requirements for the introduction of wastewater into water courses and thus also on the volume and treatment of wastewater.

By the end of 1995, a total of 37 new or amended administrative ordinances based on the fifth amendment to the Federal Water Act of 1986 came into effect. The Wastewater Charges Act stipulates that polluters must pay discharging wastewater; the amount charged reflects the amount and toxicity of the discharged substances. Wastewater charges are paid to the *Länder* and are earmarked for water pollution measures.

The fourth amendment (1994) is aimed at encouraging water polluters to invest in pollution control. The Washing and Cleansing Act sets out the legal framework that defines requirements for substances included in washing agents.

The use of substances that are hazardous to water may be prohibited or limited. The Drinking Water Ordinance includes regulations on the quality of drinking water, the obligations of operators of water supply plants, and the supervision by health authorities. In addition, the ordinance defines limit values for substances hazardous to human health, such as heavy metals, nitrates, and organic compounds, and pathogens.

Water quality is further protected by subsidiary laws under the framework Water Act, including the Chemicals Act, the Federal Emission Control Act, the Waste Avoidance Act and Waste Management Act, the Plant Protection Act, and the Ocean Dumping Act.

Protection of the sea

In 1988, the Federal government adopted a ten-point programme with the aim of improving the level of environmental protection for the North and Baltic Seas. The most important elements of the programme include faster implementation of national measures and of international obligations aimed primarily at the quicker reduction of nutrients and hazardous substances.

International co-operation for the protection of inland waters

In 1987, the International Commission on the Protection of the Rhine River adopted the Action Plan for the Rhine River, which requires parties to reduce discharge substances by 50 per cent by 1995 from 1985 levels. The overall objective is to restore the Rhine ecosystem, by the year 2000, to a condition that would result in repopulation by the higher life forms which previously inhabited the ecosystem.

In 1991, the European Council issued a directive on the Protection of Water Bodies from Nitrate Pollution from Agricultural Sources. The purpose of the directive is to reduce agricultural nitrate inputs considerably, in order to protect drinking water supplies over the long term, and to combat eutrophication of water bodies.

In 1992, the federal government signed the German-Polish Treaty on the Protection of the Transboundary Rivers of Oder and Neisse, and in 1994, Germany and ten other countries in the Danube region, together with the EU, signed a Convention on the Protection of the Danube River.

International co-operation for the protection of the marine environment

The most important international treaty on the protection of the North Sea and the Northeast Atlantic is the Convention on the Protection of the Marine Environment of the Northeast Atlantic, which was signed in Paris in 1992 by the Federal Republic of Germany and 12 other countries bordering these waters. Further international agreements include:

- London Convention on the Prevention of Marine Pollution by Dumping of Wastes and Other Matter (1972).
- Helsinki Commission International Action Programme on the Baltic Sea (1992).
- Convention on the Protection of the Marine Environment of the Baltic Sea Area (1992).
- MARPOL Convention on the Prevention of Pollution from Ships (1972).

Waste

The aim of waste management programmes in the Federal Republic of Germany is to prevent waste production in the industrial and commercial sector. The German view is that this requires Life Cycle Assessment to achieve consistent implementation of new and greater responsibility for products throughout the product's entire life cycle, *i.e.* from manufacture to disposal. The aims of the current waste management policy are defined in the framework law, the Waste Avoidance and Waste Management Act of 1986. This act establishes the following principles:

- the top priority in waste management is to avoid its generation;
- unavoidable waste should be recycled or reused wherever possible;
- unrecyclable waste should be disposed of in a manner that poses no hazard to human health and the environment.

Supplementary ordinances issued under the framework Waste Avoidance and Waste Management Act are aimed at waste reduction, waste avoidance, and waste disposal and include:

- Ordinance on the Avoidance of Packaging Waste (1991).
- Waste Oil Ordinance (1987).
- Solvents Ordinance (1989).
- Technical Instruction on Storage, Treatment, and Incineration of Special Waste (1991).
- Technical Instructions on Waste From Human Settlements (1993).

Recent refinements to the Waste Avoidance and Waste Management Act now orient it towards the promotion of environmentally compatible, closed substance cycle and waste management principles.

These principles have recently been enshrined in the Closed Waste Management Act, approved in 1994. Other key federal government statutory instruments in the area of waste management include:

- Ordinance on the Avoidance of Packaging Wastes (1991).
- Basle Convention (1994) regulating transboundary shipments of hazardous wastes.
- EC Council Regulation on the Shipment of Waste (1993).
- Waste Shipment Act (1992).

Voluntary initiatives

Voluntary initiatives by German industry are generally initiated in response to requirements set out in German law. The federal government commonly legislates targets that industry must meet; however, in keeping with the government's belief that economic benefits stem from environmental protection, the legislation does not prescribe how these goals are to be achieved. Industry is therefore free to implement voluntary initiatives that are cost-effective or may result in economic benefits, as long as the legislated goals are met.

For example, the 1991 Ordinance to the Waste Avoidance and Waste Management Act entitled the Avoidance of Packaging Waste requires both manufacturers and retailers to accept returned waste packaging and recycle it outside the public waste collection system. Seeing this as onerous and impractical, industry voluntarily established and funded Dual System Deutscheland GmbH (DSD), an organisation responsible for collecting, sorting and recycling retail packaging. The government responded to this initiative by freeing manufacturers and retailers from their legal obligation to accept returned waste packaging if they participated in the DSD initiative. The government continuously monitors the system and establishes increasingly stringent collection and sorting quotas that DSD is required to meet.

Similar voluntary initiatives have been taken for industrial packaging. For example, Bayer AG formerly used 136 different standards of wooden shipping pallets for transporting their products. This alone posed an enormous logistical barrier to recycling. To alleviate the problem, Bayer voluntarily reduced the number of standard shipping pallets to five, and to compensate the pallet supplier for the cost of recovering and recycling, Bayer agreed to pay the same price for recycled pallets as new ones. The initiative did not increase Bayer's costs, and the savings in raw materials allowed the pallet supplier to offset the costs of recycling.

As discussed in detail elsewhere in this report, German industry is also involved in the voluntary initiative established under the Responsible Care Programme.

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GLOSSARY*

Abzyme	An antibody with catalytic activity.
Activated sludge (process)	An aerobic secondary sewage treatment process using active complex populations of aerobic micro-organisms to break down organic matter.
Allosteric	A property involved in the regulation of enzyme activity, in which a substance binds to the enzyme at a position other than the active site and thus changes its shape.
Allocation	Partitioning the input or output flows of a process to the product system under study.
Antibody	A protein produced by the body's immune system in response to certain foreign substances known as antigens.
Apoptosis	Programmed cell death, as signalled by the nucleus in normally functioning cells, when age or state of cell health dictates.
Bacteriocin	A substance that certain bacteria can release which kills closely related strains of other bacteria.
Biocatalyst	An enzyme, used to catalyse a chemical reaction.
Bioconsortium	An interactive association between micro-organisms that generally results in combined metabolic activities.
Biodiesel	Vegetable oils and chemical derivatives thereof used as alternative fuels in diesel engines.
Biodiversity	The variety of all life forms, the ecological complexes in which they occur, and the ecological processes of which they are part; biological diversity at genetic, species and ecosystem levels.
Biofilm	A microbial community adhering to surfaces, usually within a matrix of extracellular polymeric substances.
Bioinformatics	The use of computers in solving information problems in the life sciences; mainly the creation of extensive databases on genomes, protein sequences, etc.
Biomass	All organic matter that derives from the photosynthetic conversion of solar energy; the total mass of living organisms in an ecosystem.
Biomimetics	A branch of biology that uses biological systems as a model to develop synthetic systems.
Chirality	A stereoproperty of some molecules that gives them left or right-handed configuration.
Chiral compound	A molecule that has an asymmetric centre and can be found in left and right-handed, non-superimposable mirror image forms (known as isomers).

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* Note: Individual chemical names, *e.g.* polycaprolactone, have not been included.

Chitosan	A polymer made of glucosamine units found in the cell walls of certain fungi.
Combinatorial chemistry	a technique whereby a random element is introduced into the automated synthesis of novel compounds thus generating many thousands of different compounds simultaneously.
Data mining	The interrogation of databases for the purpose of formulating and testing hypotheses.
Dendron dendrimer	Highly regular nanoscale globular polymers, based on a tree-like molecular structure, that can function as phase transfer catalysts *(q.v.)* or be used to immobilise reactive chemicals.
Deoxyribonucleic acid (DNA)	The molecule that generally encodes all genetic information. It consists of two strands or chains of sub-units (known as nucleotides).
Dissipative pollution	Diffuse dispersal of a pollutant, for example in a product or into the environment.
Ecology	The study of the relationships between living things and their environment.
Ecosystem	A functional self-supporting system that includes the organisms in a natural community and their environment.
Enantioselectivity	The capability of selection between two chiral *(q.v.)* isomers.
Energy flow	Input flow to or from a unit process or product system, measured in units of energy.
Enzyme	A protein which catalyses the conversion of a substrate to a product. Other than a few well-established enzymes such as papein and trypsin, most enzyme names can be recognised by the suffix-ase, *e.g.* cellulase, protease, etc.
Extreme environments	Environments characterised by extremes in growth conditions, including temperature, salinity, pH, and water availability, among others.
Extremophile	A micro-organism whose optimum growth is under extreme conditions of temperature, etc.
Feedstock	Raw material *(q.v.)* for a petrochemical process.
Flocculating agent	A chemical that effects the rapid precipitation or flocculation of a solute out of solution.
Gene	The basic unit of heredity, an ordered sequence of nucleotide bases comprising a segment of DNA. A gene contains the sequence of DNA, which encodes one polypeptide chain. The sum of an organism's genes is known as its genome.
Genetic engineering	The deliberate modification of the genetic properties of an organism by the application of recombinant DNA *(q.v.)* technology.
Genomics	The study of genomes including genome mapping, gene sequencing and gene function.
Globalisation	The geographic expansion of sales and procurement of markets, the homogenisation of consumption and production styles, and the dominant role of the industrialised countries in shaping the main direction of technological developments.
Immunoassay	An analytical technique to measure the concentration of antibodies *(q.v.)* or antigens in a solution.
Ionic liquid	Ionic solid which has been heated above its melting point (see Annex 1.2).

Lactone	The ring form of sugar acids.
Life cycle	Consecutive and interlinked stages of a product system from raw material acquisition or generation of natural resources to its final disposal.
Life cycle assessment	Compilation and evaluation of the inputs and outputs and the potential environmental impacts of a product system throughout its life cycle *(q.v.)*.
Lignin	Polyphenolic organic substances which act as binders for the cellulose fibres in wood and certain plants.
Macrophage	One of a variety of cells, present in blood, liver, etc., that ingest and break down particulate matter.
Mycorrhizae	A stable association between a fungus and the root of a plant; the root-fungus structure itself.
Oligonucleotide	A short nucleotide polymer (*e.g.* a fragment of DNA or RNA).
Oligosaccharide	A molecule made up of several simple sugar groups joined by glycosidic bonds.
Pathogen	A disease-producing agent, usually restricted to a living agent such as a bacterium or virus.
Phase transfer catalyst	A substance that increases the rate of reaction between reactants present in different physical phases (states).
Phenotype (-typic)	The characteristics of an organism that result from the interaction of its genetic constitution with the environment.
Pheromone	A hormone-like substance secreted into the environment by certain animals, especially insects.
Planktonic organisms	Organisms freely-suspended in a liquid, as opposed to those within a biofilm *(q.v.)*.
Polyketide	A large family of structurally diverse natural products synthesised by repeated cycles of condensation of thioesters; they include antibiotics, antiparasitics and anticancer drugs.
Post-translational processing	Modification of proteins after the translation of messenger-RNA into the aminoacid chain, *i.e.* by glycosylation, phosphorylation.
Proteomics	The study of gene expression with the goal of defining the entire complement of proteins expressed by a particular genome, cell or tissue type.
Quorum sensing	See Box 3.5.
Raw material	Primary or secondary material used as input to a process.
Recombinant DNA technology	The ability to excise exact segments of DNA from one species of organism and insert them into the DNA of another species.
Recombinant DNA (r-DNA)	A DNA molecule formed by joining DNA segments from two or more sources.
Recombinant (micro)organisms	Organisms whose phenotype *(q.v.)* has arisen as a result of recombination.
rDNA	See recombinant DNA.
Ribozyme	RNA *(q.v.)* molecule that is capable of catalysing a chemical reaction.
Risk assessment	Determination of potential adverse environmental health effects following exposure to pollutants and other toxic materials or to industrial processes.
RNA	A molecule with similar structure to DNA *(q.v.)* that is involved in a number of cell activities, especially protein synthesis. Some viruses have RNA as their genetic material.

Sonochemistry	Chemistry utilising the effects of ultrasound (see Annex 1.2)
Stereoselective	Pertaining to a biocatalyst that can distinguish between compounds having the same chemical composition but different structural configurations.
Stoichiometry (stoichiometric)	Describes a reaction in terms of the net proportions of reactants that are consumed and products that are produced.
Supercritical fluid	A non-aqueous material held above its critical temperature so that it cannot be liquefied.
Sustainable development	Strategies and actions that have the objective of meeting the needs and aspirations of the present without compromising the ability of meeting those of the future.
System boundary	Interface between a product system and the environment or other product systems.
Transparency	Open, comprehensive and understandable presentation of information.

A useful source of definitions in the life science area is the *Life Science Dictionary* – to be found on the Internet at: http://biotech.chem.indiana.edu/pages/dictionary.html.

The following abbreviations have been used for units throughout the report.

l	litre
kg	kilogram
bbl	barrel (of crude oil)
MPa	megaPascal (unit of pressure)
J	joule (unit of energy)
ppm	parts per million

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