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FEATURED REVIEW

Biotechnology for Industrial Sustainability

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Abstract–Until recently waste production was seen as an inevitable outcome of industrial production and processing, and a problem that could be managed by end-of-pipe and *in situ* biotreatment, disposal, or simply be ignored. However the introduction of clean, or cleaner, technology options now is focussing attention on the minimisation of materials and energy use, and waste generation, and upon recycle. Thus clean technology has emerged as a concept that is compatible with industrial sustainability, and whose environmental benefits *and* economic competitiveness have been demonstrable over a range of industrial sectors. Biotechnology is an enabling technology that offers one important route to clean products and processes; it provides powerful and versatile tools that can compete with chemical and physical means of reducing both material and energy consumption, and the generation of wastes and emissions. The wide penetration of biotechnology in industry has still to occur but many examples of its ability to deliver clean and competitive products and processes are now available particularly through the development and application of biocatalysts. The introduction of clean or cleaner processing does not necessarily entail a complete change in manufacturing strategy or the refitting of plant. Upgrading existing manufacturing processes by fitting biotechnology unit stages illustrates the opportunities for such intermediate technology. Nevertheless, for biotechnology to achieve its full potential as a basis for clean industrial products and processes beyond its current applications, innovative R&D will be needed. The successful application of biotechnology as a clean technology is illustrated in this review through a series of case studies, while the innovative nature of biotechnology in this context is demonstrated by the development and application of novel biocatalysts.

Key words: Biotechnology, Sustainability, Clean Technology, Biocatalysts, Industrial Processing, Life Cycle Assessment

INTRODUCTION

Human activities in the form of industrialisation, urbanisation, agriculture, forestry, fishing, and mineral extraction, and accompanied by the move towards globalisation of the world economy and the internationalisation of production, has led to an accelerating pace of environmental degradation. The environmental crisis as viewed by Callicott [1994] was "discovered in the industrial West in the 1960s, plastered over with regulative legislation in the 1970s, then forgotten only to return with a vengeance in the 1980s....now the focus of environmental concern is holistic and systematic, centering on the integrity of the planetary ecosystem ....it is so pervasive that it cannot be ignored". Thus the growing awareness of the need to promote sustainable development has focussed attention on the need to improve resource management and to reduce waste and pollution generation.

While sustainable development is a term open to various interpretations (the definition most usually invoked is Brundtland's: 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; Brundtland, 1987) nevertheless it conveys a basic environmental ethic that has wide public support. Thus sustainable development should provide a framework for integrating environmental policies and developing technological strategies. This review is concerned with issues relating to sustainable industrial development and the need that this imposes for continuous innovation, improvement, and the introduction of clean technologies in order to effect fundamental changes in environmental pollution and resource consumption. In short, industrial sustainability demands global vision, and a concerted move towards clean products, processes and services. I hope to show that modern biotechnology is a versatile enabling technology that already can deliver clean and economically competitive products and processes, and has the capability of ensuring long-term industrial sustainability.

1. The Paradigm Shift to Clean Technology

Pollution prevention can be conceived as a hierarchy of management options ranging through the reduction of waste at source, recycle, treatment either end-of-pipe or off-site, *in situ* remediation, or, failing all else, disposal via dumping, landfill or incineration [Bull, 1992]. Clean technology on the other hand represents 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-terms risks to human health and to the environment [Clift and Longley, 1995]. Thus clean technology defines a paradigm shift that has been recognised widely during the 1990s such that the focus is no longer on the removal of pollutants from an already damaged environment, but on the need to eliminate pollution at source; the emphasis is placed on creating rather than destroying value. Put another way, both attitudes and practices are evolving from retrospective clean-up measures to proactive clean technology. The concept of clean technology has appeared so rapidly that the conceptual agenda frequently is in advance of the necessary R&D and the means of implementation, and so the role of biotechnology in contributing to clean products and processes is examined in this review.

This paradigm shift has been brought about by several factors among them being corporate investment strategies, government pol-

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icy, public pressure, and scientific and technological advances. As a result many major companies have taken and are initiating proactive 'compliance-plus' approaches to environmental issues in attempts to secure the 'win-win' relationship of economic and environmental gain. The approach varies significantly with respect to the industrial sector, whether a company is regarded as high impact (i.e. operating relatively high up the materials chain - minerals extraction, energy, chemicals, basic processing) or low impact (i.e. lower down the supply chain manufacturing consumer products) in environmental terms, and, crucially, and whether a company is able to take advantage of *radical* in contrast to *incremental* innovations. Mature industries, exemplified by bulk petrochemicals, often are locked-in to long term technology trajectories in which case incremental and end-of-pipe developments enable continued operation along such trajectories. But even in mature industries the introduction of radical innovations can be revitalising: the combined cycle gas turbine (CCGT) is a case in point [Howes et al., 1997]. In the UK, for example, CCGT technology, made possible by the availability of natural gas and advanced gas turbines, has improved efficiency and cleanliness in power generation. A significant feature of incremental and radical innovations is that end-of-pipe technologies tend to be generic, whereas radical, clean technologies almost invariably are developed in-house and offer opportunities for strong competitive advantage and intellectual property protection.

2. Radical Innovations - What Role for Biotechnology?

Modern biotechnology is one such potent source of radical innovation for improving the environmental performance of industry, and it is widely regarded as being a dominant technology of the 21st century. It represents a considerable diversity of industrial activities based upon "the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services" [Bull et al., 1982]. The take-up of modern biotechnology over the passed 25 years has been typical of any new technology: a slow initial phase followed by a period of rapid growth (but selectively in the case of biotechnology where it has largely centered on medical applications) and entry into a mature phase of consolidation and penetration into diverse industrial sectors. The current focus of biotechnology is dominated by the human health care and agriculture sectors. However, while public attention in particular is engaged with genetically modified crops and foods and the associated questions of food safety and environmental protection, it is sometimes forgotten that the applications of biotechnology go far beyond the food and human health and are penetrating a wide range of industrial sectors. Moreover, the scientific and technological advances that are being made largely as a consequence of exploiting the enormous global markets for agriculture and medicine, inevitably spin-off occurs into innovative biotechnology opportunities in other industrial sectors; consider, for example, functional genomics, metabolic engineering, and combinatorial synthesis. The exciting features of biotechnology are its versatility and the fact that the power of the innovation continues to grow, and it is this capacity for self-improvement that enables one to forecast its very significant impact on the greening of industry [Bull et al., 1998]. Biotechnology has the capacity to impact at a global level by reducing the production of greenhouse gases and acid rain, via the use of renewable feedstocks, while on the other hand it can provide functional products such as optically active chemicals, biodegradable polymers, and enzymes that are safer, cleaner and competitive with traditional ones. It is especially important also to dispel the idea that biotechnology is fragile or scale-limited; robust biotechnology-based processes can be developed and integrated into large scale industrial operations.

3. The Adoption of Biotechnology by Industry and its Clean Impact

The adoption of biotechnology and its perception by industry as a clean technology has been patchy and perhaps slower than anticipated. Contributing to this situation are opinions that (1) end-of-pipe treatments remain the cheaper options, (2) there are long pay-back times for investment, (3) existing plant needs to be amortised, (4) the comparative cost-effectiveness of novel technology has not been established, while additional uncertainty is due to (5) a lack of information, (6) engineers not being sufficiently trained in biological sciences, and (7) companies being insufficiently aware of what their waste and pollution actually costs. An illustration of this latter point comes from an audit of the Leicestershire Waste Minimisation Initiative, an industrial club scheme recently established in the UK. The ten participating companies estimated that their combined annual waste cost was about £0.5 M but following independent waste audits the real cost was determined to be nearly £13 M, i.e. 4.5% total turnover! Potential savings of £2.6 M were identified within the first six months of the initiative by adopting sustainable industrial practices [Howes et al., 1997]. Of course, financial returns via waste minimisation initiatives of this type are achieved by picking the 'low-hanging fruit' and in order to give confidence for investing in biotechnology initiatives which will deliver longer pay-back, companies will require answers to the following types of questions:

- can biotechnology improve my or my competitor's process?
- do I have to change the entire process or just one or more unit stages?
- are biotechnological options available now or is further R&D necessary?
- can I use natural organisms or do they require genetic manipulation?
- if the latter, will the product or process gain public acceptance?
- how can I be assured that one process is cleaner than another?

Later in this review we will see how the first question can be addressed through a series of case studies taken from a variety of industrial sectors, and others will be pursued in subsequent sections.

Table 1. World-wide market share of biotechnology (BRS) for selected industrial sectors

Sectors	1996	Forecast 2005
Chemical products[a]	<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%

[a]Excludes pharmaceuticals. Source: Bull et al. [1998].

Table 2. Biotechnology market values and current contributions to clean production

Sector	Annual world market value (Billion US $)		Estimated biotechnology contribution to cleaner production (%)
	Total	BRS	
Chemicals	1726	4-6	1
Pharmaceuticals	207	21-29	5-11
Paper and pulp	900	na	3-7
Textiles plus leather	672	1.1	<1
Food processing, beverages, and animal feed	1601	22-36	1-2

na, not available. Source: Bull et al. [1998].

A major strength of biotechnology is the wide range of techniques that it comprises although no one technique is necessarily applicable across all industrial sectors. Such unique versatility has encouraged industries that previously have had no experience of deploying biological options to make serious evaluations of biotechnology. Present estimates and forecasts to 2005 for the share of worldwide biotechnology-related sales (BRS) in seven selected sectors are shown in Table 1, while current world market values and current biotechnology contributions to clean production are given in Table 2. From these data it is notable that it is in the fine chemicals, paper and pulp, and food sectors that the impact of clean biotechnology has been most pronounced so far, but clearly enormous potential exists in all seven sectors for biotechnology penetration.

Although it is undoubtedly the case that economic considerations have been foremost in determining the take-up of biotechnology, there are clear indications that responses to environmental problems have driven cleaner biotechnology in some industrial sectors. One such example is provided by biohydrometallurgical metal recovery as a more sustainable alternative to pyrometallurgy or processes such as cyanidation [Bull et al., 1998]. It is necessary to point out however that hydrometallurgy does have limitations in this context (e.g. generation of highly polluting lixiviants and large quantities of iron-containing residuals from pyritic ores) and that it will not provide solutions to all metal extraction and refining processes. Nevertheless, cases such as gold production from refractory hydrothermal deposits illustrate the advantages of bio-oxidation. Gold recovery from these latter ores is far more complex than from traditionally extracted ores because of the association of with pyrite and arsenopyrite [Haines, 1995]; this makes extraction by cyanidation difficult while ore roasting is environmentally undesirable. It is reported that the Gencor BIOX™ bacterial oxidation technology is economically competitive with roasting and alleviates the environmental problems resulting from ore roasting [Gilbertson, 2000]. Solubilised arsenic currently is removed as ferric arsenate by co-precipitation with ferric hydroxide and disposed; such an option will necessitate acceptable evidence of long term stability.

4. Case Studies

4-1. Chemicals and Pharmaceuticals

World wide the industrial chemicals business is worth US $1.4 trillion [Miller and Nagaraja, 2000]. The chemical industry has achieved a great deal in reducing pollution by adopting production-integrated environmental protection measures (for example, by developing new routes of synthesis, shifting equilibria, improving selectivity, developing new catalysts, changing reaction media, etc.; Wiesner et al., 1995), and by introducing biocatalysis into chemicals production (waste production reduced by 20% by the use of enzymes while chemicals production volume increased 4-fold during 1975-1995; Bruggink cited in Bull et al., 1998). Nevertheless, there exist huge opportunities for 'process greening' within the chemical industry. For example, data produced by the United States Environmental Protection Agency [EPA, 1995] revealed that the pollution abatement costs for six industrial sectors in the USA amounted to nearly US $1.5 billion with organic chemicals and plastic materials and resins contributing 58 and 25% of those costs respectively. Similarly the inefficiency of organic chemicals production can be judged by the 4-fold higher actual energy expenditure per ton compared to the theoretical minimum energy requirement [OIT, 2000].

A recent example of a cleaner commercial production is provided by the synthesis of the broad spectrum herbicide glyphosate [Gavagan et al., 1997]. A methylotrophic yeast, which expresses its own catalase and a recombinant glycolate oxidase from spinach, has been used to transform glycolic to glyoxylic acid which is then converted to glyphosate, N-(phosphonomethyl) glycine, in a hydrogenation reaction with (aminoethyl) phosphoric acid. The effect of introducing a biocatalytic step into the production reduces waste and the number of process steps, while the lower cost of glycolic acid compared with glyoxylic acid improved the overall production economics, the innovation provides the much sought after double dividend.

Can any logical strategy be defined for identifying particular chemicals as targets for the development of alternative, cleaner biotechnology-based processes? or, do we have to rely on *ad hoc* progress based on the priorities of individual companies? The US Office of Industrial Technology has proposed recently that the focus should not be placed on the most waste- and energy-intensive chemicals but instead upon 'chemical chains' deriving from chemical feedstocks downstream to specific chemical products [OIT, 2000]. For example, the propylene (a major global petrochemical feedstock) chain leads to polypropylene, propylene oxide, acrylonitrile, acrylates, butyraldehyde and isopropyl alcohol, and thence to an extensive range of products. In turn the acrylonitrile and acrylate sub-chains lead to products such as acrylic fibres, acrylamide polymers, acrylate paints and livestock feed additives. Alternative commercial biotechnology processes have or are being introduced for these products, the *cause célèbre* being the Nitto Chemical Company's (now Mitsubishi-Rayon) processes for polymer-grade acrylamide and acrylic acid based upon the biocatalytic conversion of acrylonitrile [Nagasawa and Yamada, 1995]. The acrylamide process, based upon nitrile hydratase of *Rhodococcus rhodochrous*, was the first successful case of a large scale biotransformation for

Table 3. Comparison of traditional chemical and innovative biotechnological routes to 7-ACA production

Chemistry	Biotechnology
1 The Process	
Produce Zn salt of cephalosporin C	Conversion of cephalosporin C to keto adipinyl-7-ACA with D-amino acid oxidase
Treat with trimethylchlorosilane to protect functional groups	Conversion to glutaryl-7-ACA (spontaneous)
React with P_2O_5 to produce imide compound	Conversion to 7-ACA with glutaryl amidase
Hydrolyse imide to 7-ACA	
2 The Pros and Cons	
Uses environmentally unfriendly and hazardous reagents	Wastewater COD increased from 0.1 to 1.7 kg per te product
Involves heavy metal salts	Residual Zn recovery reduced from 1.8 to 0 te per te product
High temperature, energy-intensive processing	Distillation residues reduced from 2 to 0 te per te product Gaseous emissions reduced from 7.5 to 1 kg per te product
	Liquid disposal (incineration) reduced from 29 to 0.3 te per te product
3 The Overall Result	
The biotechnological route reduced the percentage of process costs deployed for environmental protection purposes from 21% to 1%	

Source: Wiesner et al. [1995].

manufacturing a commodity chemical [Yamada and Kobayashi, 1996]. Although propylene-derived fibres account for a relatively small percentage of synthetic fibre production [OIT, 2000] they generate a large environmental load in terms of emissions, effluents and by-products. Considerable effort is being made to replace original chemical manufacture of fibres and polymers with biotechnology-based alternatives, or to develop completely new substitute products. Examples that use renewable rather than petrochemical feedstocks are polytrimethylene terephthalate (PTT) from glucose, and polylactic-based polymers from corn starch. The biotechnology route to PTT is particularly interesting: this polyester fibre is superior to polyethylene terephthalate but the chemical route to its synthesis from ethylene oxide is too expensive to manufacture in large quantities. The key intermediate in PTT synthesis, 1,3-propanediol, can now be synthesised directly by a recombinant organism using glucose as the feedstock in a process developed by Du Pont and Genecor [Laffend et al., 1997; Potera, 1997]. Glucose is fermented to glycerol and thence to 1,3-dipropanediol. The economics of this process are very favourable because of the 5 to 10-fold reduction in the cost of glucose when integrated into starch manufacture [Wilke, 1999]. Moreover, given that the overall mass yield of 1,3-dipropanediol from glucose currently is less than 40%, there is considerable scope for process improvement by genetic engineering to increase the yield factor. The production of PTT by this innovative route is predicted to reach one million tons by 2010.

Impressive gains in the cleaner production of antibiotics and other pharmaceutical products have been reported by several companies. Consider, for example, semi-synthetic penicillins and cephalosporins. The Kaneka Corporation has developed an all-enzymatic process for amoxicillin production from penicillin G as an alternative to a part-chemical process; the new process alleviated the formation of by-products, and colouring of the product, and also has led to improved energy efficiency. Using a similar strategy Hoechst has introduced a biotechnological route for the production of 7-aminocephalosporinic acid (7-ACA), an essential starting point for semi-synthetic cephalosporin antibiotics. Absolute environmental protection costs are reported to be reduced by 90% per tonne of 7-ACA [Weisner et al., 1995]. The former chemical synthesis and the innovative biocatalytic route to 7-ACA are summarised in Table 3.

More recently DSM also has reported a process for producing 7-aminodesacetoxycephalosporanic acid (7-ADCA) from penicillin G that combines chemical and biocatalytic steps; however, even more exciting from a clean technology point of view is the development of a complete biotechnological route to 7-ADCA and thence to novel cephalosporins such as Cefadioxil, Cephalexin and Cephradine [Van der Sandt and De Vroom, 2000]. The latter has been achieved through the construction of a recombinant *Penicillium chrysogenum* strain into which was cloned penicillin G expandase; and the development of a new dicarboxylic acid acylase (for side chain hydrolysis) which is similar to the glutaryl acylase used in the 7-ACA process. Compared with the earlier chemical process for making 7-ADCA, the new fermentation route produces greater purity of product, greatly increased energy efficiency, and very little requirement for organic solvents. Although life cycle assessments (see below) have not been published for the DSM processes, the waste volumes have been reduced by factors of 2 and 10 for the combined technology and the direct fermentation-cum-biocatalysis routes for 7-ADCA production [Van der Sandt and De Vroom, 2000]. A similar strategy for 7-ADCA production has been developed by Antibioticos S. A. In this case the *cefEF* gene encoding bifunctional expandase/hydroxylase activity of *Acremonium chrysogenum* was disrupted and replaced by the *cefE* gene of *Streptomyces clavuligerus* [Velasco et al., 2000]. The transformant synthesised high titres of desacetoxycephalosporin C which provided the substrate for subsequent aminoacid oxidase and acylase conversion to 7-ADCA.

4-2. Pulp and Paper

The pulp and paper industry is a relatively low-tech sector and is ranked among the lowest of 22 industries in terms of its average R&D investment among OECD countries [Laestadius, 1998]. In common with the food and feed industries it is regarded as a "carrier industry" that imports technologies developed in other sectors and deploys them in new or upgraded processes and products. In this context the pulp and paper industry appears to be the fastest grow-

ing market for enzymes.

Biotechnological operations that are being introduced into the pulp and paper industry with significant enhancement of cleaner processing include: biopulping, biobleaching, paper recycling, and enzymatic pitch removal. Traditional wood pulping processes involving, for example, sulphite liquor, generate very large pollution loads. Biopulping, based on the use of white-rot fungi, is being developed in many countries with promising results in both environmental and economic terms (savings in electrical energy, improved paper strength). Similarly the bleaching of brown wood pulps, traditionally achieved by chlorination, is being enhanced by enzyme treatment. Thus, biobleaching with xylanases can reduce chemical usage substantially (up to 50% for acid bisulphite pulp) without impairing fibre yield or quality. It is noteworthy that the development of genetically engineered trees to generate low-lignin pulps would greatly reduce the problem of organo-chlorine effluents resulting from the use of pulping chemicals.

A serious problem connected with the recycling of printed papers, especially those containing synthetic coating materials and printed with new generations of laser and xerographic inks, is the process of deinking. Traditional deinking processes are proving to be inadequate for such papers and are environmentally unfriendly (caustic and peroxide treatments, use of silicates). Cellulases have now been introduced to aid mechanical deinking of recycled paper. An additional benefit deriving from this biotechnology application is the improved drainage of the pulp and the consequent reduced energy requirements. Enzyme treatment removes the very fine fibres from the recycled pulp, thereby increasing the speed of paper machine operation and paper drying without sacrificing product quality [Rutledge-Cropsey et al., 1998].

The progressive introduction of biotechnology into this industrial sector promises major dividends in annual water and energy conservation. The Confederation of European Paper Industries [CEPI, 1998] reported that the quantity of water required in the production of one ton of chemical pulp fell by 75% in the last two decades and that 95% of water used in pulp and paper manufacture was now treated and returned to waterways. If water cycles in paper manufacture could be closed completely, it has been estimated that annual world-wide water use savings of 6 billion m^3 and energy use reduction equivalent to 3 million GJ could be available [Bull et al., 1998].

4-3. Textiles

The textile industry is another that comes into the category of low-tech. However, large changes have occurred in this sector as a result of globalisation and biotechnology innovation has played a significant role in maintaining the competitive advantage of many companies. Such innovations include the development of new textile fibres (from natural and synthetic feedstocks), new finishing processes (bobble removal, absorbancy properties, faded-look effect), and new production routes (genetically engineered plants for novel and coloured fibres, pest-resistance, reduced chemical fertiliser use), and have been accompanied by less polluting technologies. Lyocell is a generic name for new cellulose fibres spun from wood pulp that are superior to rayon in strength and whose manufacture is cleaner than other man-made fibres. One mechanical disadvantage of lyocell is its propensity to fibrillate during processing - this can be controlled very effectively with cellulase treatment to give a soft and laundering fast fabric [Bull et al., 1998]. In a similar application of cellulases, bobbles that often occur on cellulosic fabric surfaces can be removed, and once removed, the fabric remains stable over its lifetime. Enhancement of protein fibres also is amenable to enzyme processing which again avoid harsh chemical treatments. Among such applications are anti-felting of wool, depilling, removal of fibrin from silk fibres, softening and improved dye retention via the use of proteases.

A further application of biotechnology to textile finishing and which is environmentally compatible, has been the use of lipases to enhance the water wettability and absorbancy properties of polyester fabrics. These properties have been attained previously by alkaline hydrolysis (3 N NaOH, 55 °C, 2 h) but the lipase-based process is faster (10 min), proceeds at ambient temperature (25 °C) and does not require additional reagents. Moreover, full textile strength is retained compared to the substantial loss of strength and mass following chemical treatment [Hsieh and Cram, 1998].

A particularly successful clean biotechnology innovation has occurred for producing the 'stonewashed look' of denim. The partial removal of colour from indigo-dyed denin was previously done by abrading the material with pumice stone but has been replaced by a biostoning process based on cellulase. The benefits of biostoning are in the appearance of the garment, environmental impact, and economics - the latter being the original driving force for the change in technology. The superiority of the biostoning process has been demonstrated by life cycle assesment (LCA) and total economic cost evaluation [Bull, 1998].

Apart from the benefits of biotechnology to be found on fibre production and textile finishing, it also impacts directly on laundering. Enormous quantities of chemicals and energy are consumed world-wide on domestic and commercial laundry operations. It has been estimated that approximately 540 million laundry washes are made in households of the European Union each week (B. Jones, personnel communication). Very effective enzymes have been developed as biodetergents that will operate at the alkaline and high temperature laundry operating conditions. However, the relative energy consumption in the life cycle of a detergent including its use phase are: water heating (58% of total), washing machine operation (22%), detergent ingredients (15%), waste disposal (4%), and packaging (1%) [White, 1995]. Consequently a more sustainable approach to this activity could come from the development of high activity, low temperature biodetergents, with the resultant minimisation of energy consumption.

4-4. Food and Feed

Although the impact of biotechnology on clean products and processes in food processing and animal feed (Table 2) probably is seriously underestimated given the large BRS contribution to these sectors, the food industry has one of the lowest R&D to added value ratios of any industrial sector [Traill and Grunert, 1997]. However, it can be expected to grow further particularly as a result of consumer preferences for 'natural' products. Examples of recent clean biotechnology innovations include food preservatives produced by fermentation as alternatives to chemical agents, e.g. nisin (ex *Streptococcus lactis*) and pimaricin (ex *Streptomyces natalensis*), where the gains include a reduced number of processing stages and the avoidance of organic solvents. A recent European Commission report [Wolf and Sørup, 2000] concludes that in the food industry "se-

veral environmental problems exist which have not yet been solved satisfactorily". The latter include "large amounts of organic waste from food processing, which could be converted to valuable substances but are presently discarded…bad odours…high water and energy consumption in some processes".

So-called feed enzymes have been developed strongly for high intensity stock and poultry rearing. The use of such enzymes improves the digestability of feed and increases nutrient assimilation while reducing faeces, nitrogen and phosphorus excretion. Phytic acid (hexaphosphoinositol) is a common plant constituent, especially in seeds, but is indigestable for certain animals. The addition of phytases to feed hydrolyses the phytic acid with the release of assimilable phosphorus; this practice obviates the need to add inorganic phopsphates to feed and reduces phosphorus excretion (30% reduction of phosphate in pig faeces in phytase-supplemented animals). "In a country like the Netherlands, this would reduce the phosphate released into the environment by 20,000 tons a year. The marginal increase in the feed cost to farmers (about 0.2%) would be compensated for by a reduced levy on the discharge of phosphate" [Bull et al., 1998].

Another feed constituent used in intensive animal production is L-carnitine (essential for the transport of long-chain fatty acids). The chemical route to L-carnitine has been replaced recently by a much cleaner biotechnological process. The overall environmental load from the biotechnology route is reduced by 75% (waste water/ton), 50% (TOC/ton), >90% (incineration waste/ton) and 75% (salts/ton).

4-5. Energy

The overall scope for generating renewable energy is considerable and includes solar, wind, hydroelectricity and tidal sources. Numerous biotechnological processes either are in development, have reached pilot scale evaluation, or even are being operated on a commercial scale (usually non competitive without tax incentives) for biofuels: biodiesel (from soy, rapeseed), bioethanol (from sugar, starch), methane, hydrogen, biodesulphurisation (coal, petroleum). The intention in all cases is to replace, modify or supplement existing fuels that are more energy intensive in their production, whose use leads to greater pollution loads in the environment, and that overall make a poor contribution to sustainability. The European Union's renewable energy 'Campaign for Take-Off' [European Commission, 1997], for example, includes the following biotechnology-based targets to be achieved by 2003: 10,000 MW combined heat and power biomass installations, one million dwellings heated by biomass, 1,000 MW biogas installations, and production of five million tonnes of liquid biofuels.

Fuel ethanol is the second largest bulk chemical produced via biotechnology (approximately 13 million tons per annum). Most comparative studies have centered on the competing routes to ethanol production, but even here no comprehensive datasets are available in order to make LCAs for bioethanol. Undoubtedly in terms of carbon dioxide emission the biotechnological route is superior to the chemical route, providing as it does a net sink for CO_2; synthetic ethanol generates 1.88 te CO_2/te product while bioethanol from sugar cane and grain act as sinks (−1.46 te and −0.31 te CO_2/te product (see Bull et al., 1998). However, the somewhat intuitive assumption that bioenergy processes are sustainable needs to be thoroughly examined by LCA. Consider biodiesel: here the LCA would need to consider the conversion process itself, the downstream uses of the oil cake and glycerol by-products, pollution load, land use and the consequences of very large scale agricultural monoculture (allergenicity of rapeseed pollen; potential extirpation of important soil fertility-promoting organisms - oil seed rape does not form root symbioses with arbuscular mycorrhizal fungi) [Bull, 1996].

The potential for a hydrogen-based energy economy is being developed in many countries using a variety of technologies ranging from photovoltaic fuel cells to steam reforming of natural gas. Biotechnological options for hydrogen production include its direct production by prokaryotic organisms, and indirectly from ethanol or biogas methane. On the grounds of sustainability, hydrogen generation from renewable sources might appear to be the most attractive strategy. Once again, however, the lack of LCAs on the alternative technologies makes rigorous comparison of their environmental impacts difficult. Moreover, hydrogen is generally thought to be a clean fuel but it is important to note that its production may present detrimental environmental effects. A recent US Department of Energy life cycle assessment of hydrogen production from steam reforming of natural gas [Spath and Mann, 2000] revealed natural gas lost to the atmosphere during production and distribution as the major component of the global warming potential of the process. Consequently this factor is identified as a principal improvement opportunity irrespective of whether non-renewable or renewable methane is used. The authors announced that hydrogen production via biomass will be compared with other routes in a future LCA analysis.

5. Process and Product Upgrading

Increasing the sustainability of industrial bioprocesses can be assisted by innovative biochemical engineering, such as process intensification, that lead to greater conversion efficiencies, reduced environmental 'footprints' and so on. The question was asked earlier in this review if it is necessary to change an entire process or simply one or more unit stages, in order to enhance the cleanliness of a process or product. It is evident that the modification of extant manufacturing processes in order to remove selectively unwanted by-products, and particularly, hazardous contaminants offers a realistic and economically viable approach to clean production. Such adjunct biotechnological processing can be seen as a generic route to achieving new environmentally enhanced products.

A recent pioneering illustration of process modification involving biotechnology has been made in the manufacture of poly(aminoamide) resins which are used to impart wet-strength to paper and packaging materials [Hardman et al., 1997]. In this well-established chemical process, polymerisation is achieved with epichlorohydrin but the reaction leads to the production of unwanted haloalcohols (1,3,-dichloro and 2,3-dichloro propanols) which accumulate together with excess epichlorohydrin in the product stream and eventually end up in consumer products. Various remediation strategies (chemical process modification, physicochemical treatment of the contaminated products) were considered but a biotechnology unit stage that could be integrated into the existing manufacturing process proved to be most successful from the standpoint of generating a clean and cost effective product. The biotechnology comprised a 2-membered consortium of dehalogenating bacteria (*Arthrobacter erithii*, *Agrobacterium histidinolovorans*) that reduced the total haloalcohol concentrations in wet-strength resins from about

8,000 ppm to less than 6 ppm without affecting the performance of the resin. The retrofitted unit stage was an aerobic tank reactor operating continuously and septically and this has been installed at two manufacturing plants in Europe. An important feature about the development and implementation of this particular technology is that it was introduced into chemical plants which had not previously handled biological systems. Thus initial skepticism regarding the perceived fragility and unreliability of biotechnology was dispelled, and an extremely robust process responsive to fluctuating production needs was introduced and a new clean, commercially competitive product brought to market.

6. How to Evaluate Process Cleanliness

When arguing the case for biotechnology as a clean technology a number of caveats need to be recognised. First, biotechnological processes are neither universally nor absolutely clean - cleanliness is a comparative concept and practicality, and any biotechnology option must be judged in this light. Second, many traditional manufacturing industries, the chemical industry most particularly, are perceived and criticised as being invariably dirty and their operations unsustainable. It is worth recalling that much of the progress towards recognising and implementing clean technology originated in industries far removed from biotechnology (chemical, power, communications, photographic, petroleum; see Fischer and Schot, 1993), and that considerable advances have been made in developing novel clean chemistry [Clark, 1995; Wiesner et al., 1995]. It is imperative, therefore, to address whether, overall, biotechnological processes are significantly cleaner than competing technologies.

A large number of tools have been developed for evaluating technology impact on the environment that focus variously on management systems, risk assessment, local impact assessment, and material flow analysis. However, Life Cycle Assessment (LCA), currently is regarded as the tool of choice for assessing the cleanliness of industrial processes [Bull et al., 1998] because it demands a systematic and holistic evaluation of the total environmental load associated with providing a service by following the associated material and energy flows over the complete lifetime of a product or process (the "cradle-to-grave" scenario). Most importantly LCA enables industry to identify and evaluate opportunities for environmental enhancement of its operations. LCA provides an objective means: 1. of deciding whether a process, product or service is alleviating an environmental load or merely transferring it upstream (to resource suppliers), or downstream (to treatment/disposal); 2. of defining where in a process the most severe environmental impact is created, and 3. of making quantitative comparisons of alternative processes and competing technologies.

The development of LCA began in the 1970s and although many studies have been commissioned (see Bull et al., 1998 for an analysis of over 600 European studies) biotechnology is underrepresented, probably reflecting its relatively recent diffusion into industry and a reluctance of companies to disclose commercially sensitive information. Nevertheless, in situations where it has been used LCA has confirmed biotechnology as a cleaner and more economically attractive technology. Reference was made above to the traditional and the biostoning processes for denim processing. The results of life cycle assessments of these processes and their comparative costs are shown in Table 4.

A second example concerns the merits of using a recombinant bacterium for producing an enzyme for diagnostics application (glucose-6-phosphate dehydrogenase) compared with a low-producing wild-type bacterium. Cloning of a *Leuconostoc* G6PDH into *Escherichia coli* led to a 1,000-fold increase in productivity and a substantial reduction in pollution load (Table 5).

Table 4. LCA and economic costs (US$/100 kg) of pumice and cellulose-based stonewashing processes

Environmental effect	Pumice	Cellulase
Energy value of fuels	1.0	0.6
Chemical oxygen demand	5.2	3.1
Acidification	0.6	0.1
Eutrophication	0.2	0.1
Human toxicity: air	0.7	0.1
Human toxicity: water	2.0×10^{-3}	7.4×10^{-4}
Ecotoxicity, aquatic	4.6×10^{-2}	1.2×10^{-3}
Odour	1.9×10^{-4}	7.9×10^{-4}
Global warming effect	62.6	35.7
Environmental costs	Pumice	Cellulase
Air	8.31	4.13
Water	28.10	16.37
Waste	2.01	0.62
Total	38.42	21.12

Source: Bull et al. [1998].

Table 5. Genetic engineering to reduce pollution load

Process item	*Wildtype* G6PDH	*Recombinant* G6PDH
Broth volume, m^3	600	1
Broth constituents, kg	64,000	160
Biomass, kg	22,000	200
Water consumption, m^3	25,260	101
Air, m^3	114,000	570
Electricity, kWh	20,000	370
Steam, t	180	10
Ammonium sulphate, kg	13,000	200
Waste water, m^3	1,200	0.2
Pollution load, PE	300,000	300

PE≡one person/24 h. Source: Bull et al. [1998].

At a time when the use of genetically modified organisms in biotechnology is causing widespread concern among the public, demonstrations of this type that reveal its environmentally beneficial opportunities should receive due publicity.

It can be noted that that the application of LCA is a very effective means for comparing alternative waste management options. A recent case that illustrates this point has been presented by Dennison et al. [1998] who used LCA to determine the best practicable environmental option (BPEO) for treating raw sewage from a group of municipal plants in SE England. The impact of various management regimes including the concentration of sewage digestion, land disposal, and composting were evaluated in terms of their global warming potential (kg CO_2 equivalents) and the BPEO determined.

Finally, although LCA is taken here as the method of choice for

evaluating cleanliness, the cost of making a comprehensive LCA study can be high and this may act as a deterent to many organisations. Accordingly in a follow-up to its *Biotechnology for Clean Industrial Products and Processes* [Bull et al., 1998] the OECD currently is working on an alternative "Green Index" for comparing the relative sustainability of industrial processes. This index comprises a number of sustainability factors: reduction of energy use, reduction of raw material use, renewability of raw materials, reduction of waste, recycling of by-products, product and process safety, and innovation for continuous process improvement (S. Wald, personnel communication).

7. Impact of R&D Advances : Biocatalysis

The new generation of clean biotechnology-based processes is being driven to the greatest extent by developments in industrial biocatalysis. In the past major problems for deploying enzymes have resulted from their fragility under conditions of industrial processing, their high cost, and the requirement for large concentrations of water. Now, with the advent of genetic manipulation, artificial evolution and gene shuffling, rational manipulation of reaction conditions and enzyme presentation, and the discovery of extremozymes the customisation of enzymes for an ever growing range of industrial requirements has become a reality. The optimism surrounding biocatalysis is such that Steen Riisgaard of Novo Nordisk opines that "One day, industrial enzymes will be used in every catalyzed factory process and in every home" [Riisgaard, 2000].

Enzymes form a subset of the fine chemicals sector; they already command a large market, and are established as practical industrial catalysts (see above for some examples of current use). The advantages of developing enzymes as industrial catalysts are [Bull et al., 1999]:

(1) cleanliness compared to most chemical catalysts, particularly toxic metals;
(2) stereo- and regio-selectivity without the need to use chemical protection/deprotection steps;
(3) synthesis of pure isomers compared to racemic mixtures of products,
(4) synthesis of pure compounds compared to mixtures of by-products, thereby minimising down-stream processing;
(5) opportunities to truncate traditional chemisynthetic processes; and
(6) relatively low investment for implementing enzyme-based technology.

The search for enzymes which can be deployed under conditions of industrial processing is an on-going one and is based upon the discovery of novel natural enzymes, the design of catalysts based upon known enzymes, and the manipulation of the reaction environment. The following is a very brief indication of how developments in enzyme technology are likely to promote further penetration of biotechnology for clean products and processes (further information can be found in Dordick et al., 1998; Roberts, 1998; Bull et al., 1999; Marrs et al., 1999). Two areas are considered here briefly: customised biocatalyst design through artificial evolution, and biochemical engineering. The field of artificial evolution is developing so rapidly that its component "technologies are changing biocatalysts from an enabling tool to a lowest cost approach" [Schultze and Wubbolts, 1999].

7-1. Biocatalyst Design

The tool box for customising the design of enzymes has extended dramatically in recent years, progressing from random to site-directed mutagenesis, to artificial evolution strategies and phage display technology. Artificial evolution strategies enable biocatalytic activities (and pathway syntheses) that have not be required in the natural environment to be generated and exploited. This bottom-up design approach is in major contrast with the top-down attempts at rational design [Arnold, 2000] founded on protein structure-function relationships still awaits comprehensive databases and more sophisticated algorithms.

Directed evolution promises to be the most powerful means for developing industrial enzymes; it is a fast and inexpensive way of finding variants of existing enzymes that function more effectively than naturally occurring enzymes under specified conditions [Marrs et al., 1999]. Directed evolution experiments set defined objectives, the various stages of which are determined by the experimenter, i.e. mutation, recombination, screening and selection. The directed evolution of a bacterial esterase, via sequential mutagenesis and random recombination of positive hits, created an enzyme with a greater than 50-fold increased activity and the added benefit of delivering a cleaner option for semi-synthetic cephalosporins by circumventing the zinc-solvent procedure [Moore and Arnold, 1996]. The artificial evolution approach has also been shown to enhance the enantioselectivity of enzymes; thus, by the use of error-prone PCR and screening, the enantioselectivity of lipase was increased from 2 to 81% enantiomer excess [Reetz and Jaeger, 2000].

Gene shuffling, either of sets of a mutated gene or of famillies of homologous genes, is providing exciting results in the development of industrial enzymes. The method has been used, for example, to create fucosidase activity from a bacterial galactosidase; after only 7 rounds of shuffling and screening, an enzyme with a 1,000-fold increase in the desired activity was produced [Zhang et al., 1997]. In a process called domain shuffling, Hopfner et al. [1998] succeeded in swapping the folding subdomains of coagulation factor X and trypsin with the result that an enzyme with novel broad substrate specificity towards synthetic peptides was produced.

Similar design strategies have been deployed to affect enzyme stability, a crucial property in the context of industrial biocatalysis. Thus a protease has been rendered hyperthermostable by replacing key amino acid residues with analogous ones found in a natural hyperthermophilic archaeon [Van den Burgh et al., 1998]. This engineered enzyme maintained good activity at 37 °C and now was functional at 100 °C in the presence of denaturing agents. Protease thermostability also can be achieved by directed evolution; the recombination of 5 subtilisin variants produced an enzyme with a half-life 50 times that of the wild-type protein [Zhao et al., 1998].

Readers wishing to obtain an introduction to the methodology of artificial evolution and the biotechnology applications should consult the excellent website of Dr Francis Arnold [Arnold, 2000] which includes a compendium of published directed enzyme evolution experiments.

Phage display technology was developed as a means of identifying and isolating protein domains that bound strongly to specific ligands but it has been adapted in order to target improved enzymes. For example, phage may be linked to the substrate of a reac-

tion of interest. An enzyme displayed on the same phage particle may cleave the substrate and in so doing will cause the phage-displayed enzyme to detach from a solid support. Thus, released phage particles will, by definition, contain active enzymes.

7-2. Biochemical Engineering

The biochemical engineering inputs to industrial enzyme technology range from defining rational protocols for enzyme preparation and presentation; manipulation of the reaction environment (e.g. supercritical fluids); through chemical and mechanical procedures for stabilising enzymes (e.g. immobilisation, surface coating and imprinting); to the development of biocatalytic plastics and cross-linked enzyme crystals (CLECs) [Bull et al., 1999; Tischer and Kasche, 1999]. The principal advantages of immobilised over soluble enzymes are enhanced stability and ease of separation from the reaction mixture, thereby enabling the reuse of the catalyst and cost reductions. At this stage of development the choice between enzymes bound to prefabricated supports or CLECs will be dependent on the individual process requirements and cost-efficiencies. CLECs are crystallised enzymes cross-linked by glutaraldehyde, or similar reagents, that have zeolite-like structures; their water insolubility, mechanical robustness, resistance to proteolytic enzymes, activity in organic solvents, ease of handling and reuse promise to make them particularly attractive for industrial use if their commercial-scale production can be achieved.

Enzyme-containing plastics are being developed that have high activity and stability compared with the native enzyme, especially when reactions are made in organic media (enhanced activities may be increased by more than three orders of magnitude) [Wang et al., 1997]. Enzymes are first acrylated then solubilised in an organic solvent via hydrophobic ion pairing with surfactant molecules, and finally cross linked with a vinyl (or other) monomer to produce a plastic material that may contain as much as 50% (w/w) protein. Activity of these biocatalytic plastics is influenced by the type of monomer used and the polymerisation conditions which, in turn, influence the porosity of the plastic [Novick and Dordick, 2000]. Among the attractions of biocatalytic plastics is their ability to be formulated as particles, membranes, ribbons or coatings and subsequent use in a wide range of chemical, pharmaceutical agricultural and other industrial fields [Dordick et al., 1998].

Finally, mention should be made of one-pot syntheses in the context of clean biocatalytic production. One-pot processing offers the opportunity for minimising the number of unit stages and operations, thereby reducing reagent, plant and energy use, and bringing gains in volumetric productivities. The recent report of Cefalozin synthesis from cephalosporin C via three consecutive enzymic transformations demonstrates the potency of this technology [Fernandez-Lafuente et al., 1997]; this one-pot process removed the need to use hazardous reagents for group activation and protection, and for chlorinated solvents.

7-3. Case Histories

To conclude this brief consideration of industrial biocatalyst development and use I turn to three processes - one commercially well established, the other two embryonic but potentially large or very large scale - that indicate the success in the discovery of natural novel enzymes, and of customising biocatalysts via molecular biological techniques.

The first of these processes refers to the largest single use of enzymes in industrial processing, namely the production of high fructose syrup (HFS) from starch. In this process starch, principally derived from maize, wheat and tapioca, is hydrolysed initially with α-amylase (AA), then saccharified with glucamylase (GA), and finally the glucose is isomerised to fructose with glucose isomerase (GI). The current process conditions have been developed to take account of the limiting activities of the enzymes available, and consequently process temperatures, pH and any additions to the reaction mixture reflect these limits rather than defining ideal operating conditions [Crabb and Shetty, 1999]. Subsequently the industry is taking advantage of the discovery of novel natural enzymes and of techniques to tailor enzymes for particular processing conditions to improve the operation in both economic and sustainability terms. For example, the currently used AA has the major disadvantages of requiring Ca^{2+} ions and a pH of 6.3 or above for its activity. Site directed mutagenesis has been deployed successfully to lower the pH optimum and to increase the thermostability of the industrial enzyme. However, work from Zeikus' group [Zeikus et al., 1998] has produced natural AA from the archaeon *Pyrococcus furiosus* with very attractive properties: the enzyme does not have a requirement for Ca^{2+} and its thermostability at 98 °C is 13 times greater than the industrial enzyme. The use of natural glucamylases results in unwanted transglucosylation reactions and again site directed mutagenesis to alter the substrate specificity has alleviated this problem [Crabb and Shetty, 1999]. Finally, new glucose isomerases have been discovered that have improved properties for starch processing: the GI isolated from *Thermotoga neopolitana* has high enhanced thermostability and a temperature optimum of 95 °C [Zeikus et al., 1998]. Fructose production is favoured at high temperatures so the introduction of such thermostable GIs could affect higher fructose yields while avoiding the use of large scale chromatographic separations of glucose and fructose with overall savings in energy, materials and costs.

The second case refers to the development of a biocatalytic route for polyester adhesives production by Blaxenden Chemicals Ltd. in the UK. The existing chemical process is operated at 200 °C whereas a biocatalytic synthesis targeted for 60 °C is expected to increase the overall manufacturing efficiency. It was found that an immobilised thermotolerant lipase B preparation derived from *Candida antarctica* would catalyse the condensation of diols and diacids when the reaction was made in toluene [Binns et al., 1998]. This biotransformation process mimics the conventional chemical polyesterification and has been scaled-up for a hexane-1,6-diol and adipic acid process [Binns et al., 1999]. The biotransformation process resulted in higher energy efficiency, elimination of heavy metal catalysts and inorganic acids, and reduced water usage; the toluene can be recycled and the biocatalyst reused. Interestingly, the 'greening' of this process "is not seen as a selling argument for the company" [IPTS, 1998] but nevertheless the switch to alternative biotechnology has delivered a 'win-win' result for the company.

The final example concerns the desulphurisation of fossil fuels. Sulphur-specific transformations have been discovered in bacteria that selectively desulphurise organic sulphur-containing constituents in fossils fuels [Oldfield et al., 1998; McFarland, 1999]. The commercial exploitation of these activities has yet to be achieved but the prospects for introducing technology for petroleum desulphurisation for refinery and oil field applications are increasing as im-

proved biocatalysts are being developed. Biodesulphurisation (BDS) in this context would have obvious beneficial environmental impact, while petroleum gravity improvements and viscosity reductions could increase the value of oil reserves and reduce the costs of pipeline transport [McFarland, 1999]. Current desulphurisation technology (hydrodesulphurisation) is based on the conversion of organic sulphur to hydrogen sulphide by treating crude oil with hydrogen at high pressure and temperature. Thus, a more sustainable, lower cost technology is highly desirable in this field. Several bacteria are known that catalyse the aerobic desulphurisation of the principal organic sulphur components in crude oil, i.e. benzothiophene and dibenzothiophene (DBT). Of these organisms the International Gas Technology strain IGTS8 of *Rhodococcus erythropolis* has been intensively developed as an industrial desulphurising catalyst. Directed evolution and gene shuffling techniques have been used to improve the natural enzymes involved in DBT degradation leading to increased overall rates of degradation and to a broadening of the organo-sulphur substrate range. Truncating the pathway can lead to the accumulation of intermediates such as 2-hydroxyphenylbenzene sulphinate, dibenzothiophene sulphoxide and sulphone that could serve as feedstocks for surfactants, phenolic resins or adhesives [McFarland, 1999]. Research over the past decade has resulted in the activity of the recombinant *R. erythropolis* IGTS8 increasing 200-fold which, it is claimed, places it within an order of magnitude of that required for a commercial BDS process. A number of engineering problems associated with reactor design, separations and byproduct recovery require solutions before commercial BDS becomes a reality but there is every reason to expect that the biocatalyst specifications will be met through the application of the new generations of recombinant DNA technologies.

8. Actions and Some Implications

The OECD report on *Biotechnology for Clean Industrial Products and Processes* [Bull et al., 1998] considered the following points to be the central findings to its enquiry and for consideration by the main stakeholders, i.e. government, industry, the public, and the scientific community:

(1) global environmental concerns will drive increased emphasis on clean technology;

(2) biotechnology is a powerful enabling technology for achieving clean products and processes,

(3) measuring cleanliness is complex but essential - LCA is the best available tool for the purpose,

(4) the main drivers of industrial biotechnology are economic, government policy, technical feasibility,

(5) greater penetration of biotechnology for sustainable industry will require joint R&D efforts by government and industry,

(6) to reach its full potential biotechnology will require continued R&D investment,

(7) there is a strong need for harmonised and responsive regulations and guidelines for biotechnology,

(8) market forces provide powerful incentives for achieving cleanliness objectives,

(9) government policies are the most decisive factor in the development and industrial use of clean biotechnological processes, and

(10) communication and education are necessary to gain penetration of biotechnology for clean products and processes.

Nevertheless, there remain serious difficulties and hindrances attending the innovation of biotechnology across industry. In a more recent survey of process-integrated biocatalysts in selected companies in Europe, Wolf and Sørup [2000] identified the following problems: lack of knowledge and know-how, a perception that biotechnology does not work, unqualified staff, low R&D intensity, a lack of company data on its environmental performance, difficult economic situations, and difficulties in assessing the benefits of bioprocessing. Wolf and Sørup conclude that for policy purposes it is necessary (a) to enlarge and publicise the scientific-technical knowledge base; (b) to raise the awareness and motivation of management staff; (c) to improve the qualification and motivation of technical staff; and (d) to increase the transparency of benefit/cost ratios of new biotechnologies and to reduce their transaction costs.

Undoubtedly biotechnology can make a major contribution to the goal of industrial sustainability but government and industry together will need to communicate with various target audiences to evince that industry and the environment can be compatible partners. Companies exist to create wealth and they have always looked to the economic bottom line to gauge what advantages they can gain from adopting new technologies. But now the new concept of the *triple bottom line* developed by John Elkington and his colleagues at SustainAbility Ltd. [Elkington, 2000] is a more appropriate one for evaluating the biotechnology option for clean and sustainable industrial development. Triple bottom line evaluation forces attention not only on whether a process or product is economically viable, but also asks if it is environmentally sound and if it is socially responsible. If sustainable industry is to become a reality, the stakeholders (industry, government, public) must work together to maximise the triple bottom line performance; as Elkington has remarked: "to this end, we not only need new forms of accountability but also new form of accounting….we must find accurate, useful and credible indicators of economic prosperity, environmental quality, and social justice". Many companies now are reporting annually on their sustainability performance and have established business principles against which to appraise their activities (for example, see The Shell Report, 2000; Shell International, 2000). Such reporting is becoming a crucial activity for industry; it has started to be surveyed globally by UNEP and reporting guidelines were issued in June 2000 [GRI, 2000].

Clean technology is being promoted most rapidly and aggressively in economically powerful, industrialised countries and this has a number of wider implications. Clean technology will be broad ranging and a part of the globalisation phenomenon; it will impact on mature and emerging industries in different ways (e.g. constraints of being locked-on to long-term technology trajectories vs. implementation of radically innovative technologies); the latter has consequences for intellectual property protection (e.g. non or poorly protectable generic remediation technology vs. novel patentable clean technologies); world trade and the position of small companies and developing countries (e.g. greener purchasing policies). Whereas attention has been focussed primarily on the cleaner production/product side of the equation, companies are increasingly concerned about their supply chains and the issue of 'greener purchasing'. Greener purchasing devolves strict environmental standards onto suppliers of raw materials, components, etc.; the result may be a general gaining in cleaner practices but also may bring

short- or medium-term difficulties for small suppliers and for developing countries whose current technological capacities may not yet be compatible with this wider trading framework.

Elkington [2000] points to a cluster of *sustainability revolutions* that currently are impacting on industry, they include: life cycle technology shifting from products to functions; time scales changing from shorter to longer; transparency progressing from closed to open; and corporate governance evolving from exclusive to inclusive with regard to environmental security. If biotechnology is to fulfil its potential contribution to industrial sustainability, effective collaboration between all of the stakeholders in these matters will be essential.

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