

Strategies for Sustainability

Pharmaceutical companies are looking at ways to improve their sustainability across all areas of their business, from R&D to sales and distribution.

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A 'sustainable' business needs to satisfy three criteria: it must be economically viable, socially justified and environmentally acceptable. This article explores how the pharmaceutical industry is adopting a holistic approach to continuously reducing its environmental footprint while continuing to deliver benefit to the patient. The environmental component of sustainability relates not only to manufacturing but also to research, product development, sales and distribution. Figure 1 shows the challenges and opportunities currently

facing the industry (1). Rapid progress is now being made in most of these areas.

Research & Development

In 2010, spending on R&D by the global industry was \$127 billion. This large-scale activity has its own sustainability challenges relating both to the operation of the research facilities and to staff travel in a globally organised business. In fact, more energy is consumed by the industry's research laboratories, mainly in operating fume cupboards, than by its factories. These issues are now

being addressed within global business programmes for reducing energy consumption. Most pharmaceutical research companies have set themselves targets to dramatically reduce their energy demand as well as cutting their greenhouse gas emissions.

The objective of R&D activity is to produce a regular stream of new medicines, which must now undergo a rigorous environmental risk assessment. Environmental evaluation is also needed to meet the requirements of other legislation. For example the eventual

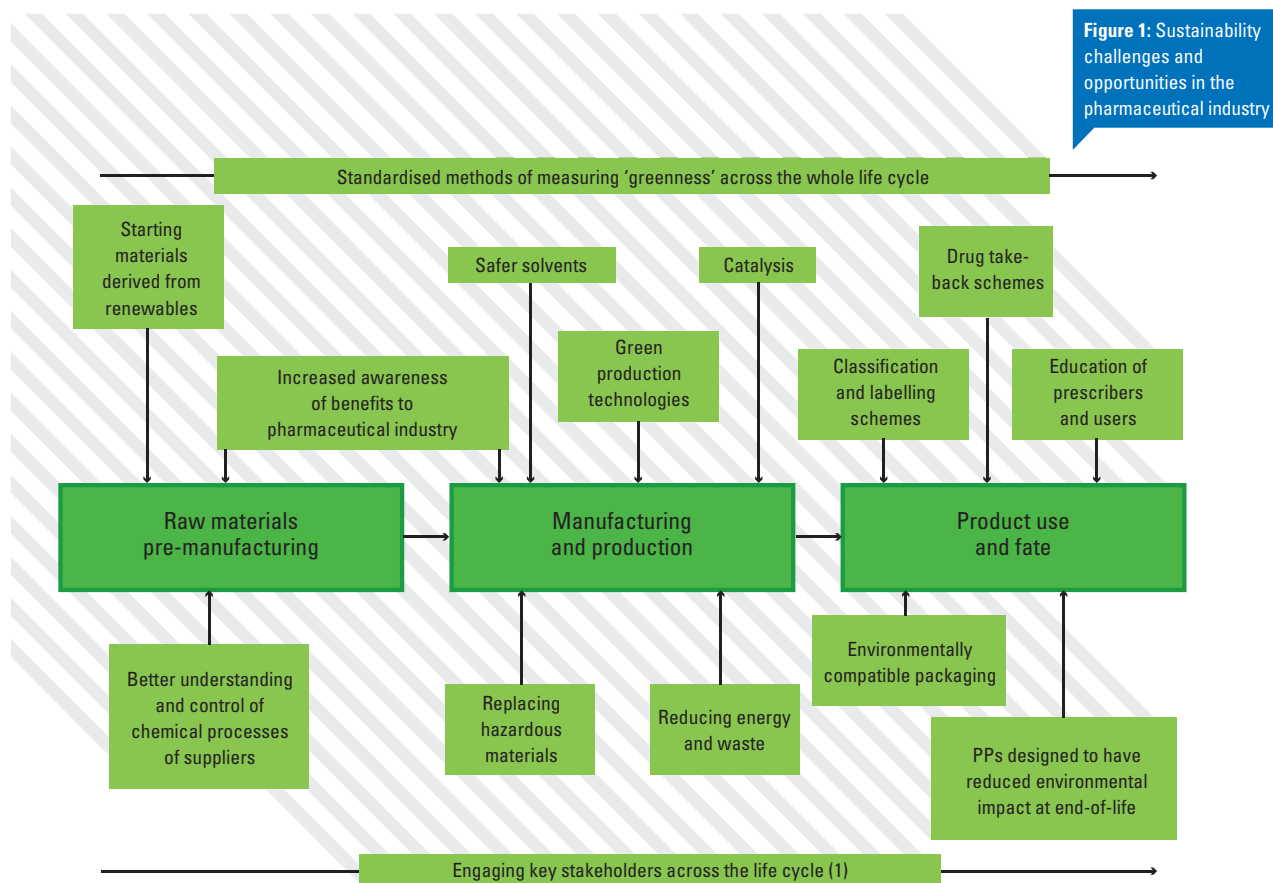


Figure 1: Sustainability challenges and opportunities in the pharmaceutical industry

manufacturing plant will need to meet the consent conditions imposed by the local environmental regulator, which could apply to the product as well as any waste materials involved in its manufacture. Some companies like AstraZeneca have proactively set their own stringent targets for site emissions (2).

Although the total mass of finished product produced by the industry is small, a large proportion of this subsequently enters the sewers following excretion from patients. Not all of this is subsequently removed during waste water treatment. Consequently, very low residues of many pharmaceuticals can now be detected in most parts of the aquatic environment.

It is generally believed that these concentrations are far too low to pose any threat to human beings and no immediate threat to wildlife (3,4). There is still relatively little information on long term impacts on wildlife, but the emerging conclusion from a major review of the ecotoxicological data for the EU Knowledge and Need Assessment on Pharmaceutical Products in Environmental Waters Project (KNAPPE) suggests that, with one or two exceptions, significant long term wildlife effects may also be minimal (5).

Nevertheless, like many industrial sectors, the pharmaceutical industry is continually seeking to decrease the impact of its products on the environment. Current progress in R&D could lead to subsequent generations of drugs leaving lower residues in the environment. This does not mean that the industry is simply trying to make its products biodegradable. Biodegradable medicines can have other problems related to 'shelf life' and pharmacokinetics and, unless they degrade extremely rapidly, will still leave residues in the environment due to their constant input from multiple point sources. In addition, our knowledge of chemical degradation in the environment is currently far too rudimentary to be able to predict with any confidence how a new synthetic chemical could be modified to retain its

pharmacological effectiveness and safety while increasing its rate of environmental decay. Research continues to be carried out in this area, but it is unlikely that this will lead to any significant advances in drug design in the near future. There are many other ways, however, by which environmental residues can be reduced.

Biopharmaceuticals

All of the major research pharmaceutical companies are interested in the emerging area of 'biopharmaceuticals'. These compounds, which are frequently based on proteins, now comprise up to 30 per cent of new compounds under development. They have the advantage of being very specific in their mode of action. They need very low doses for effective treatment and will usually be broken down to inert substances before excretion by the patient. It is thought that environmental residues of such medicines will be significantly lower than that of current medicines.

Manufacturing

Pharmaceuticals are produced in relatively small quantities, from a few kilograms per year for some anticancer drugs, to a few hundred tonnes per year for more widely used medicines, and a few thousand tonnes per year for some analgesics. This is in contrast to some bulk chemicals where 1,000 tonnes per day production is common. Unlike the majority of 'bulk' chemicals however, most pharmaceuticals are very complex organic molecules that have to be constructed using multiple synthetic steps, often involving the isolation of intermediate products. As a consequence, process efficiency has historically been very low (6).

Driven by cost and sustainability issues, research pharmaceutical companies have in recent years become industry leaders in the introduction of green chemistry and technology techniques into their process design. Companies have now developed sophisticated systems to ensure that potential environmental consequences, as well as health and safety considerations, are taken into account in the selection of reagents and solvents.

Sustainability metrics are routinely used to compare alternative process routes (7). This has led to major improvements in the efficiency of these complex syntheses, and pharmaceutical companies such as Merck regularly win US Presidential Green Challenge Awards. The major companies are also now collaborating at the American Chemical Society Green Chemistry Roundtable, sponsoring research that should lead to even more sustainable synthesis routes (8).

Solvents comprise the largest part of the waste produced in pharmaceutical manufacture, and extensive recycling and reuse of solvents is undertaken to minimise resource consumption. Solvents that cannot be reused or further recycled are incinerated, usually in installations which can recover the energy. Although the formulation aspects of manufacture do not involve chemical synthesis, they can generate significant waste streams, mainly associated with the cleaning of equipment to avoid cross contamination. These wastes are, however, readily treatable using modern technologies, such as reverse osmosis and activated carbon.

Minimising packaging has also been the focus of much effort in the industry, although this has sometimes been impeded by other, often desirable, legislative requirements; for example, loose tablets now have to be encapsulated in blister packs and pharmaceutical labels in the EU must now include information in Braille. These regulations have unfortunately resulted in increased amounts of packaging.

As discussed above, the pharmaceutical industry is now beginning to explore the new area of biopharmaceuticals. Few of these have yet reached the patient and their manufacture at full scale will provide new sustainability challenges. The active ingredients, often protein based, are too large and complex to be synthesised by conventional chemical techniques. As a result, current biopharmaceuticals tend to be manufactured in cell cultures using fermentation methods which can produce very large volumes of very low concentration effluents.

In recent years there has been an increasing tendency for more and more of the manufacturing operations in research pharmaceutical companies to be contracted to third parties. One aim of outsourcing is to increase sustainability by improving operational efficiency and saving costs.

Most drugs have a relatively short useable patent life, usually of less than 10 years. In order to get a new drug onto the market as soon as possible, the manufacturing plant needs to be established before the product has received approval from the regulators. If the product is extremely successful, this manufacturing plant may not then be big enough to cope with demand. But if the product fails to gain approval from the regulator the plant will not be needed at all, nor will it be as useful after patent expiry. It is thus a more sustainable practice to contract the manufacturing of the product to a number of external suppliers, who can expand to cope with any unexpected demand.

In the last 10 years, the contract fine chemical manufacturing sector has become very experienced, highly competent, cost efficient and successful. Since contract manufacturers are focused on chemical manufacture, they can be more efficient in their use of energy and resources than their pharmaceutical customers.

Contractors in newly industrialised countries (NICs) such as Brazil, China and India currently have a major competitive advantage as a result of very low (although increasing) wage costs. Concerns often remain, however, about quality, security of intellectual property and health, safety and environmental issues. Recent investigations show very high concentrations of active pharmaceutical ingredients in the effluent from a waste water treatment plant serving drug manufacturers in Patancheru in India, and similar findings in China have highlighted the potential problems (9,10). This reinforces the need for pharmaceutical companies to take great care both in their selection and particularly in their continued performance monitoring of contractors.

At present, most pharmaceutical outsourcing remains with contractors in the developed world.

Sales and Distribution

Initially, sales and distribution may appear to have little relevance to sustainability, but there are significant challenges to be overcome in this area. Research companies need to ensure that any new medicine is brought rapidly to the attention of as many doctors as possible. This has traditionally been achieved through the use of sales representatives that call personally on doctors to provide them with information.

A major company will usually have a large sales force whose only efficient means of transport will be the motor car. Companies have been tackling this in two ways. The immediate objective is to improve the efficiency of road travel by using more efficient vehicles and extending driver training to include eco-driving techniques. In the longer term e-commerce techniques may dramatically reduce the need for direct contact between the sales force and the individual doctor.

Abbott has already committed itself to going 'carbon neutral' with its US fleet of vehicles. The company's 6,000-car fleet represents nearly 11 per cent of its overall global emissions and this commitment will take 180,000 metric tons of emissions out of the air – the equivalent of taking 12,000 cars off the road.

To fulfil patient demand, a product has to be distributed from the factory to the pharmacy. This inevitably leads to the emission of greenhouse gases, even if distribution is not a major emitter. As an example, only 10 per cent of AstraZeneca's total greenhouse gas emissions come from freight transport. But improvements are nevertheless being made. Bulk transport with final packing of products at the marketing companies has reduced demand for freight whilst efforts have simultaneously been made to use more environmentally friendly packaging options.

For example, volumes can be reduced significantly by using slip-sheet techniques in air freight rather than conventional pallets. Furthermore, reusable blankets have replaced polystyrene boxes for temperature-controlled transport wherever possible. Selection criteria for road hauliers and airlines take into account both age and type of fleet as a matter of course. Trials are also underway into the use of container ships to replace road and airfreight where possible. This has the potential to reduce greenhouse gas emissions while simultaneously increasing security and providing more consistent storage conditions.

Finally, considerable efforts across the industry are going into the elimination of wastage in the distribution system. This is much more complicated than it sounds. Unlike most other commodities, it is essential for patient care that their medicine is always available from the pharmacy whenever they need it. Demand for a particular medicine, however, is variable and difficult to predict since the requests come from a very large number of pharmacies.

In the past, this problem was dealt with by ensuring that sufficient stocks were held by the manufacturer, distributor and pharmacy to meet all requirements. Most pharmaceuticals, however, have a limited shelf life and this policy has resulted in significant amounts of out-of-date medicines being continually returned to the manufacturer for destruction. This is both wasteful and costly, and serious attempts are now being made, using more sophisticated 'lean' engineering and 'just-in-time' delivery systems, to eliminate unnecessary stock in the supply chain. This will reduce overall wastage while ensuring continuity of supply to the patient.

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