

ENVIRONMENTAL REVIEW

Our ongoing challenge is to continue to manage our environmental impact as we grow our business. Our global performance objective is to drive continuous improvement in the sustainability of all our activities by, among other things, economising on the use of natural resources and working to eliminate pollution.

CLIMATE CHANGE

In common with most businesses, our potential impact on climate change arises from the greenhouse gas emissions from energy use at our facilities, from other in-house activities and from the various means of transport we use. However, we also face an additional challenge since some of our asthma therapy products use propellant gases that potentially contribute to ozone depletion and global warming.

Asthma is a common, often debilitating illness that can be alleviated by breathing in medication from a small aerosol called a pressurised metered dose inhaler (pMDI), which uses propellant gases to deliver the medicine. When CFCs, the gases used originally in pMDIs, were identified as ozone-depleting gases, we worked to develop alternatives. Our *Turbuhaler* dry powder inhaler, launched in 1987, does not require a propellant gas, but it is not suitable for all patients. We therefore developed and are introducing alternative propellant gases for our pMDIs, which have no ozone depletion potential and significantly less than half the global warming potential of the CFCs they replace. Although these HFA (hydrofluoroalkanes) propellants still have some impact on climate change, there is an international consensus that there is no safer alternative for patients.

A strong track record

At the formation of AstraZeneca in 1999, we began to take action firstly to reduce the rate of growth and then to stabilise the emissions of CO₂ from our facilities. This was achieved by a combination of energy efficiency measures, investment in combined heat and power plants and purchasing energy from low or zero carbon sources. By 2003 the upward trend in emissions from these sources had been arrested and by 2005 emissions had fallen to their 2001 level. By 2007, our absolute greenhouse gas emissions from all sources (including products) had fallen by 67% compared with 1990. (The Kyoto Protocol target is a 5% reduction by 2012).

The growing challenge

The process of developing, manufacturing and distributing innovative medicines to patients is increasingly complex and uses more and more energy, both in our facilities and in travel and transport. Controlling transport-related emissions remains a significant challenge. Although we have invested in electronic communication systems and expanded their use, this has had limited impact on emissions from these sources. We are now investing heavily in advanced driver training to improve both safety and efficiency associated with road travel and we are increasingly using a range of hybrid and alternative fuel vehicles.

Since 2000, the greenhouse gas emissions associated with our products has declined as we are phasing out CFC-based pMDIs and our market share of these products has changed due to patent expiries. During 2006, however, we received approval to market a new asthma treatment, *Symbicort*, in the US, where over 30 million people suffer from this debilitating disease. Our new therapy provides rapid and effective asthma control in a pMDI containing HFA propellant. The launch during 2007 of this therapy in the US, the world's largest pharmaceutical market, will inevitably lead to an increase in emissions of HFAs as more and more patients benefit from the new medicine. Despite the potential climate change implications, we believe that the expanded treatment choice and potential benefits that *Symbicort pMDI* offers asthma sufferers outweigh the potential impact it will have on the environment.

Next steps and future targets

We have identified areas of our business where further improvements can be made to reduce our emissions of global warming gases. These include, amongst other things:

- > Implementation of further energy conservation programmes, particularly related to fume cupboards in laboratories.
- > Implementation of green technology principles in our process design.
- > Further investment in greener energy supply from external power suppliers.
- > Exploring the potential for further investment in low carbon and renewable energy options at our sites.
- > Investment in 'cleaner' vehicles.

Our fundamental challenge continues to be reducing our emissions at a pace that equals or exceeds our rate of business growth. We will continue to work hard to manage our impact, and our new climate change target aims to ensure that our absolute emissions in 2010 will be no greater than they were at the start of the decade and 40% less than they were in 1990. Although the greenhouse gas emissions from our business operations will continue to fall, as a result of the launch of *Symbicort pMDI* in 2007, we will not be able to continue to achieve the reductions of total greenhouse gases (including emissions from products) that we have delivered each year since 2000. We are committed to achieving our 2010 target without compromising our ability to provide new inhalation therapies that bring benefit for patients. Therefore the climate change objectives approved by the AstraZeneca Board in 2005 require very substantial efforts to be made across our business to produce, by 2010, an absolute reduction of 12% in global warming emissions from all sources other than pMDIs, when compared with 2005.

PHARMACEUTICALS IN THE ENVIRONMENT (PIE)

In recent years, improved analytical techniques have resulted in pharmaceutical residues being detected at low concentrations in the aquatic environment. There is general agreement among scientists in academia, industry and government that, although variable, the levels found are too small to pose any significant risk to human beings or to cause immediate or short-term harm to aquatic life. More information is needed to determine if there are any long-term effects and AstraZeneca is actively involved in this research, as described later in this section.

Our approach

The environmental profile of AstraZeneca's new pharmaceuticals is assessed prior to applying for government approval and, at a minimum, consistent with applicable regulatory regimes. We are committed to conducting our assessments based upon the best available science, which is continuously evolving. For example, the United Kingdom and Sweden have carried out major reviews of the scientific data relevant to the potential impact caused by pharmaceutical residues in the environment. New Environmental Risk Assessment Guidelines have now been introduced in the European Union and are being revised in a number of other regions, particularly in Canada and Japan. We continue to work with the relevant pharmaceutical industry trade associations to provide expert input to the current public consultations.

ENVIRONMENTAL REVIEW CONTINUED

In anticipation of these new guidelines, and as an element of our internal PIE-related initiatives, we have reviewed the environmental risk assessments for our existing products and, where appropriate, carried out further studies to replace previous default values with measured data.

We are committed to making this environmental risk data, together with available information on our existing products, publicly available via the Swedish Doctors Prescribing Guide, FASS.se website, using the voluntary disclosure system introduced by the Swedish Association of the Pharmaceutical Industry (LIF). A total of 27 substances with environmental data are now included in this database. The system was developed by LIF and a number of Swedish stakeholders, in conjunction with expert representatives from international pharmaceutical companies, convened and chaired by AstraZeneca. In association with the Association of British Pharmaceutical Industries we are also helping the Environment Agency for England and Wales to evaluate the risks of the existing medicines on their priority action list.

In addition, we have introduced an Environmental Risk Management Plan that will accompany all new medicines through the development process and will enable all relevant environmental data to be available at all key decision points.

Our research

Scientists at our Brixham Environmental Laboratory in the UK are at the forefront of research in this field, working both independently and in collaboration with other companies, leading academics and regulatory bodies to advance PIE-related research. We recently invested a further \$24 million in new laboratories at the site to improve the facilities for evaluation of the environmental fate and persistence of pharmaceuticals.

As the research moves forward, the understanding of some of the complexities of this issue improves. There was an initial concern that all pharmaceuticals might have long-term environmental effects that were not predictable, by extrapolation, from short-term studies. However, as evidence accumulates it appears that this may only be an issue for a small number of substances that demonstrate 'atypical' effects. For example, AstraZeneca has undertaken a full fish life cycle study on tamoxifen that showed

significantly less toxicity than might have been predicted for a hormonally acting compound. It also appears that even some closely related substances with the same mode of action can show very different environmental profiles.

This has been observed with the beta-blockers, atenolol and propranolol, for example, where atenolol shows significantly lower toxicity to fish compared with propranolol. Our research has also demonstrated that natural photo-degradation, caused by sunlight, can be a powerful factor in the removal of pharmaceutical residues from the environment. For example, there is evidence that around 70% of propranolol can be destroyed this way. It seems, therefore, that all medicines should be evaluated on a case-by-case basis in these respects, rather than being grouped together as a single class or classes.

To eliminate any potential environmental impact, pharmaceuticals ideally would break down rapidly on contact with water. However, to be effective medicines, they must be stable enough to get to the part of the body where they need to be active, without deteriorating along the way. Our increased focus on biological products (which tend to be metabolised by the body or rapidly degraded in the environment) and targeted therapies with shorter treatment regimes will contribute to fewer residues, but balancing the needs of the patient with the potential environmental impact will continue to be a challenge.

Based upon work conducted to date, we have no scientific basis for believing that our manufacturing discharges pose a significant threat to the environment. However, we will continue to conduct internal evaluations for the purposes of identifying future research needs and guiding internal risk management decisions. In the longer term, we will continue to work to ensure that the development and application of our evaluation techniques remains consistent with the evolving science, and that our manufacturing activities remain protective of human health and the environment. One example of our commitment is the commissioning of a \$36 million state-of-the-art biological treatment facility at our Avlon Works in Bristol in the UK as well as improving effluent treatment at other facilities.

More information about commitment to managing our environmental impact, and our performance, is available on our website, astrazeneca.com/responsibility.