

Pharmaceuticals in the Environment

Issue

Pharmaceutical products are designed to cure and treat disease, and to help people be healthy. However, like many foods and nutritional supplements, they are not always completely absorbed or broken down by the body. Residues of the pharmaceutical or its breakdown products (i.e., metabolites) may be excreted as part of normal biological processes. Sewage treatment systems are not always able to remove these substances and the residues sometimes pass through treatment facilities and enter rivers, streams or lakes. Residues of some pharmaceuticals may persist in the environment.

Pharmaceutical products may also enter the environment from unused products being disposed of either into the sewerage system or in landfill sites.

Some pharmaceuticals have been detected in the environment at very low levels. Pharmaceuticals have probably been in surface waters since people first started taking medicines many years ago. However, as a result of advances in analytical techniques, only now can they be detected.

Published studies to date report no appreciable risk to human health for the GSK compounds considered, but we are aware of increasing reports of studies on pharmaceuticals indicating potential impacts on aquatic life. GSK is committed to ensuring that our products do not adversely affect people and the environment. We carry out state-of-the-art environmental testing on all our pharmaceuticals and use these data in risk assessment models to evaluate potential for harm to human health and the environment. Evaluations of our compounds do not indicate an adverse impact to public health or the environment from post-patient releases to the environment. GSK continues to work with industry groups and regulators to develop the science and methodologies to evaluate our products and management practices on an on-going basis.

GlaxoSmithKline Position

1. GSK acknowledges that the presence of low levels of pharmaceuticals in the environment is a stated concern of some parties and we are working to address the issues. We are committed to ensuring that our products do not adversely affect people, aquatic life or the environment in general.
2. As a science-based company, we have an in-depth understanding of the chemical and biological attributes of our pharmaceutical compounds. We leverage the results of research by academic, industrial and government organisations and contribute our expertise to advance knowledge of the environmental impacts of pharmaceuticals
3. GSK tests and assesses for potential effects on the environment to meet current regulatory requirements and GSK's internal global Environment, Health and Safety Standards for all new Pharmaceutical & Consumer Healthcare products before they are launched. In addition, GSK reviews the evolving science in this area to ensure that we have the best possible understanding of potential risks and ways to minimise them.

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4. We regularly update our testing protocols for new and existing GSK pharmaceuticals as knowledge and testing methods improve. We conduct tests to determine effects from both short-term (acute) and long-term (chronic) exposures of aquatic organisms to pharmaceuticals in the environment, as appropriate for a particular compound based on its environmental behaviour.
5. If environmental risk assessments indicate areas of concern, GSK will communicate with affected parties such as regulators, patient groups, and others to find methods to manage these in the context of the health benefits derived by patients.
6. GSK will work with relevant regulatory agencies around the world responsible for pharmaceutical product approvals to ensure that sufficient data and assessments are available to allow an understanding of the therapeutic benefit and environmental impact of our products.
7. At the same time, we will make information on the environmental hazards and impacts of our products readily accessible.
 - Data sheets on our pharmaceutical products can be found on www.gsk.com
 - GSK publishes environmental data, assessments and related topics in the scientific literature
 - GSK works with regulators to ensure that relevant precautions are included on labels and in information to patients.
8. GSK will constantly strive to avoid harm to public health and the environment by determining the environmental fate and effects of new compounds as part of GSK's evaluation and risk mitigation measures to manage any adverse impacts of our products.

Background: Summary

The presence of active pharmaceutical ingredients (APIs) in the environment from post-patient excretions is being reported in the peer-reviewed scientific literature by scientists around the world. Improvements in analytical capabilities now allow even very low levels of these materials to be detected. APIs are being detected in drinking water, surface waters such as rivers and lakes, ground waters, and sediments. Comparisons of these measurements with predicted no effects levels for people find that the levels of pharmaceuticals present in the environment are too low to pose any short-term (acute) or long-term (chronic) risk to people. However, questions about the potential for long-term (chronic) effects on aquatic life for multiple compounds or certain classes of compounds are now being raised.

Concerns about the possible effects of chemicals, including household products and pharmaceuticals, is developing into a high profile issue in Europe, the United States, Canada and other countries around the world. The issue becomes of increasing concern as population density and consumption of pharmaceuticals continue to increase.

The science underpinning this debate is still under active development. GSK is involved with industry trade associations such as the Pharmaceutical Research and Manufacturers of America (PhRMA), the Association of British Pharmaceutical Industries (ABPI), and the



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European Federation of Pharmaceutical Industry Associations (EFPIA) to advance the state of the science.

Background: Detail

The issue of the potential environmental impact of pharmaceuticals, though often presented as an emerging one, is not new. The US Food and Drug Administration (FDA) has regulated pharmaceuticals in the environment (PiE) in the USA since 1977 through the environmental review process for New Drug Applications submitted to the FDA. In Europe, guidelines for Environmental Risk Assessments (ERAs) that accompany Marketing Authorisation Approval Applications for new drugs have been available in draft since 1996, with the most recent draft issued in January 2005. Other actions by regulatory agencies are increasing. In Canada, a requirement for environmental assessment is in place and a specific environmental risk assessment (ERA) process for pharmaceuticals is under development. In Sweden, a classification scheme for pharmaceuticals based on their environmental hazard and risk characteristics is being implemented and the results are being published in the national prescribing guide for doctors. The UK Environment Agency has issued a Position Statement declaring pharmaceuticals in the environment to be a priority, and the Agency is now working with the ABPI to agree a way forward. In the US, an interagency task force dealing with pharmaceuticals in the environment has been formed that includes the US Food and Drug Administration (US FDA) the US Environmental Protection Agency (USEPA), the US Geological Survey (USGS), the Centers for Disease Control and Prevention (CDC) and the National Oceanographic and Atmospheric Administration (NOAA) as well as other agencies.

Since the late 1980's, GSK, as part of industry groups, has been working with drug approval regulatory agencies to ensure that potential environmental impacts of pharmaceuticals are understood and minimised. PhRMA has developed a state-of-the-art model (the Pharmaceutical Assessment and Transport Evaluation, or PhATE™, model) to facilitate a deeper understanding of potential environmental distributions of pharmaceuticals at a local or regional level in the US. GSK has been using PhATE™ and other similar models developed independently by other groups for Europe to identify potential impacts of GSK pharmaceutical products entering the environment through patient use. As part of its product stewardship activities, GSK continues to monitor and utilise as appropriate the latest scientific studies and findings to improve its risk mitigation in this area.

All of these emerging considerations have led GSK to develop a policy position on pharmaceuticals in the environment that is publicly available on the GSK web-site (www.gsk.com). In 2004, GSK conducted interviews with interested external parties on this issue. Since those meetings, GSK has also conducted a series of internal stakeholder consultations to further refine and develop its position.

This public position paper now lays out our response and our commitments as a company. We already test our products according to currently recognised and established procedures. Results of these tests are used to calculate Predicted No-Effect Concentrations (PNECs) which are compared to Predicted or Measured Environmental Concentrations (PECs or MECs) to assess risk. The risk assessments that have been carried out to date using these models, combined with currently available human and environmental fate and effects data and methods, indicate that GSK pharmaceuticals in



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the environment do not appear to present an appreciable risk to humans or the environment.

In addition, although the issue of pharmaceuticals in the environment primarily deals with APIs, we may also evaluate other components of our products with regard to their potential environmental impact. For example, chlorofluorocarbons (CFCs), which are used as propellants in some of our aerosol products, are ozone-depleting chemicals. There is work in progress to eliminate CFCs from all GSK products, and the GSK position on CFCs is provided in another GSK position paper. Assessments on potential impacts from manufacturing operations, while considered of high importance, are not addressed here, as these operations are within direct GSK control and are managed according to local regulatory requirements and GSK Global EHS Standards.

The science underpinning this debate is still under active development. Although standard laboratory testing methods have been employed for many years and the results used in environmental assessments, field studies carried out by academic and government organisations are now highlighting the gap between extrapolations from laboratory data and actual removal performances in wastewater and drinking water treatment plants and in the environment. In addition, there are few data on the environmental hazards of many older pharmaceuticals, and the distribution and degradation (i.e., the "fate") of pharmaceuticals in the environment are not yet well understood or characterised. The potential environmental effects of pharmaceuticals will undoubtedly vary between different compounds and with different types of organisms, making them hard to predict. Recent concern has focused on effects from long-term (chronic) exposures of APIs to aquatic organisms that are more difficult to test for than shorter term, acute exposure effects. In addition, environmental relationships and models developed and used for industrial chemicals often give misleading results for pharmaceuticals; however, these deficient models are the ones being used by regulatory agencies, which may then classify compounds as more hazardous than they actually are. Therefore, GSK is part of industry efforts to develop better environmental fate and effects models. The results of these studies will be used to develop strategies for environmental fate and effects testing schemes and risk assessment procedures that are relevant and cost-effective.

Approved: January 2006

A publication of Corporate Environment, Health & Safety



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Further Background Information

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