

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 completely remove these substances and the residues sometimes pass through treatment facilities and enter rivers, streams or lakes. To a lesser extent pharmaceutical products may also enter the environment from unused products or via pharmaceutical manufacturing discharges.

While some pharmaceutical residues have been detected in the environment at very low levels, published studies to date, including the WHO's 2011 Technical Report on *Pharmaceuticals in Drinking Water*, indicate they are unlikely to affect human health at the levels detected. However a few studies indicate some potential for impact on aquatic life.

GSK is committed to ensuring that our compounds do not adversely affect people or the environment. We carry out state-of-the-art environmental testing on all our pharmaceuticals and use these data in risk assessments to evaluate potential for harm to human health and the environment. The results of these assessments indicate no 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 continually evaluate our products and management practices.

GSK's Position

1. GSK acknowledges that the presence of low levels of pharmaceuticals in the environment is an area of concern for some parties and we are working to build a deeper scientific understanding of the issues in order to address these concerns. 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 performs environmental risk assessments to meet current regulatory requirements as well as our own 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.
4. We regularly update our environmental testing protocols as knowledge and testing methods improve. We conduct tests to determine effects on organisms from both short-term (acute) and long-term (chronic) environmental exposures to pharmaceutical residues.

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5. If environmental risk assessments indicate areas of concern, GSK will work with appropriate stakeholders, 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. We make information on the environmental hazards and impacts of our products readily accessible to interested parties in the following way:
 - Safety 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 supports voluntary and responsible programmes dealing with safe disposal of unused medicines.

BACKGROUND

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 extremely low levels of these materials to be detected. Some API residues are being detected in drinking water, surface waters, such as rivers and lakes, ground waters, and sediments. Comparisons of these measurements with current Predicted No-Effect Concentrations (PNECs) for humans 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 have been raised.

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

Regulatory Oversight

The issue of the potential environmental impact of pharmaceuticals, though often presented as an emerging one, is not new. However in recent years regulatory agencies have increased their scrutiny and activity in this area:

- 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 since 1996, with the most recent update issued in January 2006. In Sweden, a classification scheme for pharmaceuticals based on their environmental hazard and risk characteristics has been implemented and the results are being published in the national prescribing guide for doctors.

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- In Canada, a requirement for environmental assessment is in place and a specific environmental risk assessment (ERA) process for pharmaceuticals is under development.

Industry Response

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.

GSK's Approach

All of these emerging considerations have led GSK to establish this policy position on pharmaceuticals in the environment that is publicly available on the GSK web-site (www.gsk.com). GSK continually benchmarks, refines and updates our position by conducting interviews with interested external parties as well as internal stakeholder consultations.

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

The Science

The science underpinning concerns about potential risks 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 highlighting a gap between extrapolations from laboratory data and actual removal performances in wastewater and drinking water treatment plants and subsequent fate in the environment. There are also few data on the environmental hazards of many older pharmaceuticals, and the distribution and degradation 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.

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. GSK is therefore 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, insightful and most appropriate for pharmaceuticals.

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Unused Medicines

Although patient use is the primary source of pharmaceutical residues in the environment improper disposal of unused or expired medicines is also a contributing source. GSK encourages proper and safe disposal by patients and supports the use of approved voluntary 'take-back' programs in the communities and countries where they are available.

We endorse the prescription pharmaceuticals proper disposal guidelines developed by the U.S. White House Office of National Drug Control Policy. We also support the SMARxT Disposal initiative. This is a public awareness campaign for safe disposal guidelines and is a unique public-private partnership between the U.S. Fish and Wildlife Service, the American Association of Pharmacists and the Pharmaceutical Research and Manufacturers of America.

GSK welcomes and supports all initiatives that protect people and the environment by keeping unused medicines from entering the ecosystem.

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