Roche Position on Pharmaceuticals in the Environment (PIE)

The situation

Pharmaceuticals were developed to treat or prevent human disease. Their use results in releases to the environment that cannot be completely prevented. Pharmaceuticals can enter the environment in a variety of ways: the manufacturing process, improper disposal of unused medicines, and from patients who take medicines that eventually pass through the human body. Patient use is universally recognized as the primary contributor.

With the ever increasing sensitivity of analytical methods pharmaceutical active ingredients and their metabolites have been detected in the environment in very small concentrations by various researchers in many countries. They are present in rivers, lakes and streams, as well as in the water we use in our homes. The presence of these biologically active compounds has raised concern regarding their potential human health and environmental impact, concern about the potential effects associated with long-term exposure of aquatic organisms and humans, and uncertainty about the possible effects of mixtures of many pharmaceuticals simultaneously present in the environment in trace amounts.

The need to act

As releases of pharmaceuticals into the environment cannot totally be avoided, it is necessary to assess their potential impact in a scientific and differentiated way.

From a public health perspective, the risk posed to humans by exposure to the low concentrations of a variety of pharmaceuticals in the environment must be thoroughly investigated and evaluated. The quantities that have been found in the environment are in general far below the level at which they have been shown to have a therapeutic or adverse effect in humans. Indeed, various publications suggest that even a lifetime of consuming drinking water containing these trace concentrations of pharmaceuticals would not correspond to one single daily therapeutic dose of the respective active substances. Nevertheless, potential long-term effects of low concentrations of these substances and potential combination effects need to be researched further, in order to strengthen the fact base and decide on the necessity of future protective measures.

From an environmental perspective, research continues at an elevated rate as scientists attempt to better understand the environmental fate and effects associated with the small concentrations of pharmaceutical compounds present in the environment, especially in water. Studying these potential impacts is very complex due to the large variety of aquatic species, the broad range of chemicals and the combinations of pharmaceuticals and other substances that may be present in the water. To date, studies concur that the low levels of pharmaceuticals generally found in the water do not cause short-term impact to aquatic life. More and more scientific studies are being conducted in an effort to further understand this issue and to evaluate the potential effects associated with long-term exposure of aquatic organisms. There are indications that certain hormones (in particular sex

hormones) and other substances exhibiting hormone-like activity may have detrimental long-term effects on aquatic populations. While Roche has historically been involved in the manufacture of synthetic sex hormones, such products are not part of our current product portfolio.

From a regulatory perspective, many parts of the world, including the European Union, Switzerland, the United States and Australia, soon also Japan and Canada, require that environmental risk assessments be conducted in order to obtain a marketing authorization for a new drug product. These assessments are designed to predict the amount of pharmaceuticals that may enter the environment, along with the impact that the presence of these compounds may have.

Additional regulations have been enacted to address the protection of the environment associated with emissions from manufacturing facilities and waste disposal. For example, several member countries of the European Community have already established collection systems for unused medicines, and patients are advised not to throw away or flush their unused medicines, but to return them using established collection systems. In the United States, the government has issued guidelines advising patients not to flush their unused medicines, but rather to dispose of them in the household trash and use "take back" programs where they are available.

Roche position and objectives
Roche in principle believes that releases of pharmaceuticals into the environment are undesirable and therefore should be minimized whenever possible. Those releases that still occur must be assessed in a scientific and differentiated way.

Pharmaceuticals were developed to treat or prevent human disease. Roche believes that the evidence available today indicates that the benefits derived from the use of pharmaceuticals far outweigh the risks arising from their presence in trace amounts in the environment.

Roche believes that the risk to human health associated with exposure to the levels of pharmaceuticals currently found in typical waters (surface, ground and drinking water) is extremely low. This is primarily based on the wealth of human health data generated as part of the medicines approval process.

Roche strongly supports the need for continued research into the possible effects associated with long-term exposure to mixtures of pharmaceuticals, especially on aquatic organisms. We believe that a collaborative effort, which includes regulatory authorities, industry and academia, will provide the most benefit. As a company, we remain committed to obtain reliable data on our products to use as a basis for scientific risk assessment accepted by regulators world-wide and for the implementation of appropriate risk management measures to minimize the amount of our products entering the environment.

Roche action
Roche is actively engaged in a number of initiatives to better understand the PIE issue and to minimize the amount of our products that are released to the environment. We participate in several international and national bodies dedicated to studying the impact of trace chemicals including pharmaceuticals in surface waters and groundwater. These organizations include

- the Swiss Experts' Commission for Environmental Toxicology;
- the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC);
- The EU NOMIRACLE Research Programme on assessing effects of multiple stressors;

- the German START Research Programme on reducing the occurrence of pharmaceuticals in drinking water (2007 – 2008);
- the EU ERAPharm Research Programme (2004 – 2007);
- and others including scientific societies and congresses.

Roche is actively contributing, supporting and working to better understand the human and environmental health impacts of PIE and to promote appropriate approaches to wastewater treatment.

Roche manufacturing facilities are designed and operated to ensure that, as far as practicable, the active pharmaceutical ingredients are not discharged into the wastewater (especially from equipment cleaning processes). Additionally, manufacturing emissions are treated in wastewater treatment plants, where a significant part of this waste is degradable and thus readily removed via biological mechanisms. If risk assessments require it necessary, Roche facilities pre-treat wastewater using additional technologies prior to discharge. For example, one of our newest manufacturing facilities in Mexico is being equipped with an ozone forced-oxidation system designed to effectively eliminate the pharmaceutical active substances manufactured there before they reach surface waters. In other facilities, the active molecules are chemically destroyed before the process wastewater is released to the treatment plant.

Roche has also established financial incentives to ensure that unused or outdated products are returned by retailers and others in the supply chain, and our policies require that any returned or waste pharmaceutical product be incinerated rather than disposed of in landfills. Roche participates in pharmaceutical take-back programmes in the EU and supports the use of existing local take-back programmes in the US, as well as the implementation of a farther reaching program on the national level.

This position paper was adopted by the Corporate Sustainability Committee on April 25, 2008 and entered into force the same day.