

ENVIRONMENTAL FOOTPRINT OF PHARMACEUTICALS: THE SIGNIFICANCE OF FACTORS BEYOND DIRECT EXCRETION TO SEWERS

CHRISTIAN G. DAUGHTON*¹ and ILENE S. RUHOY²

¹Environmental Sciences Division, National Exposure Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, 944 East Harmon Avenue, Las Vegas, Nevada 89119; ²College of Osteopathic Medicine, Touro University Nevada, Henderson, Nevada 89014, USA

Abstract—The combined excretion of active pharmaceutical ingredients (APIs) via urine and feces is considered the primary route by which APIs from human pharmaceuticals enter the environment. Disposal of unwanted, leftover medications by flushing into sewers has been considered a secondary route—one that does not contribute substantially to overall environmental loadings. The present study presents the first comprehensive examination of secondary routes of API release to the environment and for direct but unintentional human exposure. These include bathing, washing, and laundering, all of which release APIs remaining on the skin from the use of high-content dermal applications or from excretion to the skin via sweating, and disposal of unused and partially used high content devices. Also discussed are the health hazards associated with: partially used devices, medication disposal practices of consumers, and interpersonal dermal transfer of API residues. Understanding these secondary routes is important from the perspective of pollution prevention, because actions can be designed more easily for reducing the environmental impact of APIs compared with the route of direct excretion (via urine and feces), for reducing the incidence of unintentional and purposeful poisonings of humans and pets, and for improving the quality and cost-effectiveness of health care. Overall, unintentional exposure to APIs for humans via these routes is possibly more important than exposure to trace residues recycled from the environment in drinking water or foods.

Chemotherapeutics in Sweat {Page 2503} - Excretion of chemotherapeutics via sweat is well established, but its overall significance as a secondary exposure route for others is not. That chemotherapeutics are excreted via sweat is reflected by its becoming recognized as a primary cause of a variety of adverse cutaneous effects during chemotherapy (e.g., doxorubicin), including hand-foot syndrome (hand-foot skin reaction) [47,48] and hyperpigmentation and alterations to nails. The specific formulation can enhance the excretion of the API via sweat. But with respect to unanticipated exposure, this route of excretion holds the potential for promoting subsequent incidental exposures for others and poses higher risks than for other drugs because of the extreme cytotoxicity and mutagenicity of oncolytics. Excretion via sweat undoubtedly also plays a role in the development of hypersensitivity to certain other drugs because it ensures skin contact with drugs not intended for dermal application. Early studies indirectly measured the excretion of chemotherapeutics via sweat by mutagenicity assays. For example, a 1988 study showed that sweat collected from patients treated with cyclophosphamide and other antineoplastics showed greater mutagenicity than controls 8 h after treatment [49]. A mean concentration of methotrexate in sweat was measured as 725 ng/ml (mean maximal concentration of 1.7 mg/ml), calculated as translating into excretion of 300 mg per day through sweat [50]. Other studies provide strong indirect evidence that sweat conveys chemotherapeutics outside the body. These studies have focused on studies of occupational exposure [51], where bedding becomes contaminated and serves as a route of exposure for health care workers and especially those working outside hospitals, such as home care providers [52]; workers in laundry facilities were noted as having the potential for higher exposures to antineoplastics than oncology nurses during the handling of bed sheets.

Although direct exposure to APIs via contact with the sweat of others has unknown significance, the APIs excreted from the skin of those taking medications (including those undergoing chemotherapy) have the potential to be released fully from the entire body in public spas and swimming pools. This is a scenario where inappropriate or unwanted dermal contact could occur to concentrations higher than those in waters from the ambient environment (e.g., .1 ppb, mg/L). For those undergoing polypharmacy, the release of multiple APIs likely would occur.