Time to Limit Antibiotic Pollution

The use and misuse of antibiotics is a major driver behind the drug-resistance problem, but large environmental discharges of antibiotics from pharma manufacturing can also contribute. It’s time for companies to live up to their ethical responsibilities.

By Johan Bengtsson-Palme, doctoral student at the Department of Infectious Diseases, The Sahlgrenska Academy, and D. G. Joakim Larsson, Director of the Centre for Antibiotic Resistance Research (CARe) at the University of Gothenburg, and Professor in environmental pharmacology at the Department of Infectious Diseases, the Sahlgrenska Academy, University of Gothenburg, Sweden.

Over the last decade, antibiotic resistance has put increasing pressure on human healthcare and is estimated to account for 700,000 deaths every year (1). The use (and misuse) of antibiotics in both human medicine and agriculture is a well-known cause of resistance; a much-less discussed driver is the environmental discharge of pharmaceuticals (2). Both the development and spread of resistant bacteria in the environment can be promoted by antibiotic selection, and so release of antibiotics into the environment can accelerate the problem. Importantly, in contrast to the use of antibiotics, environmental discharges are not associated with any benefits – only risks.

For a long time, the subject of environmental pollution with antibiotics has been neglected – presumably because the potential impact of the problem has not been recognized. Slowly, awareness is growing, but we need improved national and international regulation – and established limits for environmental releases, if we are to make a difference. At the moment, there is little public information about where and how medicines are produced, because of a lack of transparency in the production
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chain. This also means that it is difficult to know which companies are making an effort.

In our view, companies producing and formulating antibiotics have an ethical responsibility to minimize the discharge of antibiotics into the environment. With available treatment options for bacterial infections deteriorating rapidly, we need to act fast. Unfortunately, the current systems for assessing risks associated with pharmaceutical pollution do not account for resistance promotion (3). Ecotoxicological data for antibiotics is scarce and, when such data exist, the identified effect concentrations are often higher than those that kill many bacterial species, and hence do not protect against resistance selection.

Recently, we broadly estimated the concentrations that promote resistance based on the EUCAST (European Committee on Antimicrobial Susceptibility Testing) database on the antibiotic susceptibility of clinical isolates (4). We based our estimates on the fact that a given antibiotic concentration that kills or inhibits growth of some bacterial species will, by consequence, be selective under at least some conditions. Thus, the lowest inhibitory concentrations reported are also the upper boundaries for selective concentrations. The actual selective concentrations are likely to be even lower – but exactly how much lower is still not known. By accounting for limited sampling of species and the extent of available data, we used the upper boundary concentrations to predict no effect concentrations (PNECs) for each antibiotic.

These PNECs for resistance selection can be applied in regulatory contexts, and may eventually be refined or supplemented with experimental data as they become available (5). The recent O’Neill report on antimicrobial resistance, commissioned by the British Government, specifically highlights the urgent need for enforceable regulations on antibiotic discharges (6). The concentrations we report can be used by local authorities to define emission limits for antibiotic-producing factories, or for pharma companies to assess and manage risks for resistance selection associated with their own discharges. They also fill an important knowledge gap to make the proposed environmental certificates within the good manufacturing practice framework for antibiotics concrete. Similarly, further development of environmental criteria as part of public procurement processes for antibiotics, as implemented by Sweden and considered by the WHO, will eventually require defined discharge limits. There are also strong incentives to introduce evaluations based on scientific data in the environmental risk assessment of antibiotics within the guidelines of, for example, the European Medicines Agency.

Demands for the sustainable, ‘green’ production of pharmaceuticals have already been raised and this is likely to accelerate, which means that pharma companies should be prepared for increased pressure in the future in the form of sharpened procurement criteria and new legislation. Companies with foresight can benefit by making early efforts to reform their production chains towards green manufacturing to get ahead of the enactments to come. A transformation to documented sustainable production may have other benefits for pharmaceutical producers too, by providing environmentally friendly products to conscious customers, which could set responsible companies apart from the negligent. Most companies will want to avoid distrust associated with not taking action (see the “Bad Medicine” report by Sum Of Us (7) for an example of this). With a large number of proposed discharge limits now at hand (4), we think the time is ripe to take action.

References