Executive Summary

Pharmaceuticals can be introduced into water sources through the discharge of treated sewage effluent from individuals and patients who have used these and from agricultural runoff containing livestock manure. The risks associated with the presence of specific pharmaceuticals in a water source will vary depending upon factors such as the extent of discharge into water bodies, the pharmaceuticals prescribed, used or manufactured in the area, water treatment and the size of the population in the catchment.

In 2007, wca Environment conducted a desk-based review for the Drinking Water Inspectorate (DWI) and concluded that there was unlikely to be a significant risk from pharmaceuticals discharged into drinking water sources (Watts. C *et al.*, 2007), but that a small-scale survey would be useful given the paucity of measured data in drinking water at that time. Such a study was carried out by Boxall *et al.* (2011) who detected benzoylecogonine, carbamazepine (CBZ), carbamazepine-10,11-epoxide (carbamazepine epoxide; CBZ-EP), ibuprofen and naproxen in treated water. Authors concluded that the levels of pharmaceuticals in drinking water in England do not pose a appreciable risk to human health, as they were orders of magnitude lower than therapeutic doses.

The objective of this project was to carry out a risk assessment of the pharmaceuticals measured in the previous study, by comparing potential intake values from drinking water with toxicologically-derived health-based guidance values.

Following the risk assessment paradigm, a critical assessment of the literature was carried out to identify the hazards of each pharmaceutical. Pharmaceutical companies were also approached for additional toxicological data.

Following hazard identification, hazard characterisation was carried out, by first identifying a point of departure (PoD) in the form of a no observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) from the retrieved experimental animal or human epidemiology data. For some of the pharmaceuticals, i.e. for metabolites benzoylecogonine and carbamazepine epoxide, no data were retrieved. In such cases, alternative approaches were considered, including the use of Quantitative Structural Relationship Analysis (QSAR) modelling or the Threshold of Toxicological Concern (TTC) approach. Once the PoD was determined, uncertainty factors (UFs) were assessed on a case by case basis and used to calculate an acceptable daily intake (ADI).

The exposure assessment for pharmaceuticals via ingestion of drinking water was calculated based on the maximum and median concentrations of pharmaceuticals reported by Boxall *et al*., (2011) and default assumptions of body weight and daily water intake for adults, children and infants.

During risk characterisation, the intake of pharmaceuticals in drinking water was compared against the ADI and the hazard quotient (HQ) calculated. The margin of exposure (MOE) was also calculated as part of the risk communication phase.

NO(A)ELs were determined for all five pharmaceuticals, either from experimental data (carbamazepine, ibuprofen and naproxen) or via QSAR modelling (benzoylecogonine and carbamazepine epoxide). Chemical-specific UFs for all pharmaceuticals were derived, as in most instances, the default UFs of 100 were deemed inappropriate based on the data from which the NO(A)EL was derived.

The intakes of all pharmaceuticals for all receptors (adults, children and infants) were all below the calculated ADIs and the HQ were all <1. Moreover, the MOEs for all chemicals indicated it would be unlikely that they would be of concern.

Overall, when carrying out a human health risk assessment based on the levels of specific pharmaceuticals in drinking water samples reported by Boxall *et al.* (2011), using default exposure parameters for adults, children and infants, and when using toxicological endpoints as the PoD, then the levels of these pharmaceuticals measured in drinking water are not anticipated to pose an appreciable risk to public health.