Response to Comment on "Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999−2000: A National Reconnaissance"

We thank Ericson et al. (*1*) for their careful review and thoughtful comments on the synthetic hormone data presented in our recent publication summarizing the results from the USGS nationwide reconnaissance for pharmaceuticals and other organic wastewater contaminants (*2*). Their efforts have helped raise the awareness of the difficulties in accurately measuring these compounds at the low concentrations that occur in the environment and reinforce the need for continued research in the area of analytical methods development for synthetic hormones.

Ericson et al. (*1*) raise concerns that reported synthetic hormone concentrations, in particular 17α-ethinyl estradiol (EE2), were substantially higher than anticipated and suggest that this difference may be due to interference by natural organic materials that could not be resolved by the analytical method used. Briefly, the method was adapted from techniques developed for analysis of biological fluids and involved isolation of 14 natural and synthetic steroid and hormone compounds from unfiltered, aqueous samples (pH adjusted to 2) using continuous liquid−liquid extraction (CLLE) with methylene chloride. The residues were derivatized to form the methoxamine/trimethylsilyl ethers of the steroidal compounds. Analysis was by GC/MS in both full-scan and selected-ion monitoring (SIM) modes. To achieve the necessary sensitivity, however, only the SIM data were used.

Ericson et al. (*1*) indicate that the method used was similar to previous research (*3*, *4*) where significant interference from both natural and synthetic organic materials were reported. The authors were aware of these potential interference issues and took precautions during sample preparation to minimize such interferences from occurring. CLLE with methylene chloride was used to minimize co-extraction of potential interferents that can take place with solid-phase extraction (*5*) used in these previous studies (*3*, *4*).

Qualitative identification of each compound in the SIM mode was based on the following four criteria: (a) matching of retention time within 0.02 min of values obtained from analysis of authentic standards, (b) presence of the molecular ion of the target compound, (c) presence of at least two additional qualifier ions (at least one of which was a fragment of the parent compound structure), and (d) matching of ion ratios within 50% for the two qualifier ions. A compound was considered to be detected and a concentration quantified when all of the above criteria were met. The above procedure is consistent with that used by laboratories at the National Institute for Drug Abuse and the U.S. Environmental Protection Agency. Three deuterated surrogate standards (cholesterol-d_7, 17β-estradiol-d_4, and testosterone-d_3) were added prior to derivatization to evaluate method performance.

Shortly after the publication of our stream reconnaissance study (*2*), we discovered that select concentrations for EE2 and mestranol, which had been rejected as having potential interferences based on the above criteria, were not corrected in the final published database. Seven concentrations of EE2 (ranging from 0.023 to 0.831 μg/L) and four concentrations of mestranol (ranging from 0.034 to 0.197 μg/L) were erroneously published. In the initial report (*2*), the frequency of detection, maximum concentration, and median detectable concentration for EE2 were reported as 15.7%, 0.831 μg/L, and 0.073 μg/L, respectively. Similarly, the frequency of detection, maximum concentration, and median detectable concentration for mestranol were reported as 10.0%, 0.407 μg/L, and 0.074 μg/L, respectively. The corrected frequency of detection, maximum concentration, and median detectable concentration are 5.7%, 0.273 μg/L, and 0.094 μg/L respectively for EE2 and 4.3%, 0.407 μg/L, and 0.017 μg/L respectively for mestranol. The frequency of detection of reproductive hormones, reported as 40% in the initial report (*2*), has been corrected to 37%. The percent of total measured organic wastewater contaminants, by general use category, reported as 0.88% in the initial report (*2*) has been corrected to 0.69%. The erroneous concentrations for EE2 and mestranol that have been identified herein have been corrected in our corresponding data report (*6*).

The EE2 results of our study are consistent with those of previously published investigations (*1*), being infrequently detected in only about 6% of the streams sampled. The median detectable concentration, defined as the median concentration in samples in which that compound was detected, was provided to give a better indication of measured concentrations than simply providing the maximum concentration found. Thus, in the 5.7% of the streams where EE2 was detected, the median detectable concentration was 0.094 μg/L. Because the "nondetects" are not reflected in the median detectable concentration value, it cannot be considered a good measure of the central tendancy of the data for all samples and therefore should not be used in the U.S. Food and Drug Administration's Environmental Introduction Concentration (EIC) calculation method as was done by Ericson et al. (*1*).

As noted by Ericson et al. (*1*), the selection of sampling locations, which was targeted at sites susceptible to contamination by organic wastewater contaminants, and the analysis of unfiltered water samples, representing contributions from both suspended material and dissolved phase, may have contributed to the synthetic hormone concentrations reported in this study being higher than those reported in previous studies.

The U.S. Geological Survey greatly appreciates these review comments. These types of reviews play a key role in the development of analytical methods to increase the accuracy and sensitivity of measurements of natural and synthetic hormones and other environmental contaminants of emerging concern.

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