NACWA
A Clear Commitment to America's Waters

October 9, 2008

Mary Smith
Director, Engineering and Analysis Division
U.S. Environmental Protection Agency, Ariel Rios Building (4303T)
Office of Science & Technology, Office of Water
1200 Pennsylvania Avenue, N.W.
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Via Electronic Mail

Dear Mary:

As the leading representative of publicly owned wastewater treatment agencies in the United States, the National Association of Clean Water Agencies (NACWA) is committed to ensuring that the analytical test methods used to assess water quality and permit compliance under the Clean Water Act are both scientifically sound and reasonably implementable by municipal laboratories. NACWA is concerned with the recent release of two EPA methods (1694 and 1698) for the analysis of pharmaceuticals and personal care products (PPCPs). Though these methods are not approved/ promulgated in 40 CFR Part 136, they will no doubt be interpreted as EPA 'endorsed' methods and be used for regulatory purposes. In fact, in California, monitoring requirements in discharge permits using the new methods are already being pursued by the state.

NACWA is concerned with the performance of these methods during the single lab validation study that was conducted and the fact that there has been no opportunity to publicly comment on the methods or the validation study. NACWA's members are working to gain a better understanding of the multiple methods currently in use for quantifying PPCPs and steroids and believe that it is premature to rely upon any single method, particularly one that has not been subjected to rigorous, multi-laboratory validation regarding method accuracy and precision and for some analytes requires the use of expensive and uncommon instrumentation, when less expensive alternatives may be substituted and yield equally precise results.

NACWA is asking that EPA issue a statement which acknowledges the existence of other methods to analyze these constituents and outlines the limitations of methods 1694 and 1698. Chief among our concerns with the two methods is their poor performance in a single lab validation study, particularly Method 1698. Despite strong recommendations from the Federal Advisory Committee on Detection and Quantitation Approaches and Uses in Clean Water Act Programs, to establish data quality objectives (DQOs) for the programs that use these methods before developing and/or publishing analytical methods, these methods were subjected to a validation study without DQOs to define what would or would not be acceptable performance. DQOs would have

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better defined the extent of validation necessary (i.e., the number of labs, the number and types of matrices, the types of labs, etc.) and would have also determined whether the limits for calibration verification, initial precision and recovery (IPRs) and ongoing precision and recovery (OPRs) printed in the methods are acceptable for the uses of the data. Even without consideration of the need for DQOs, the methods clearly have not been sufficiently validated for use in Clean Water Act programs.

NACWA also offers the more specific comments in Attachment A for your consideration. NACWA understands that these methods are performance-based and that some of our comments can be addressed through method modifications in the performance-based context. Nevertheless, these issues only serve to further compound the problems associated with the use of these insufficiently validated test methods.

Again, NACWA is asking EPA to issue a statement or otherwise clarify that there are other methods that can reliably be used to analyze for these constituents and that Methods 1694 and 1698 have several limitations when applied in a Clean Water Act context. Given the increasing focus being placed on the presence of these PPCPs in water, NACWA believes it is critical that the clean water community have available robust, valid analytical methods that can be conducted at more than just a few of the most advanced labs in the country. NACWA understands that these methods have not been promulgated and added to 40 CFR Part 136 and are therefore not "EPA Methods", but implementation has already shown that state regulators and others are eager to require clean water agencies to monitor for these substances and these methods will no doubt begin appearing in Clean Water Act permits.

Thank you for the opportunity to share our concerns with the methods.

Sincerely,

Chris Hornback
Senior Director, Regulatory Affairs

cc. James Hanlon, Director, Office of Wastewater Management, U.S. Environmental Protection Agency Office of Water

Attachment A

Method 1694

NACWA feels that this is generally a sound method capable of quantifying a large number of compounds. The method, however, suffers from its attempts to cover such a long list of analytes, resulting in the poor single laboratory validation recoveries observed for some compounds. NACWA's specific comments are outlined below:

- The extraction cartridge described in the 1694 method is fairly expensive and large in terms of size and resin mass. This cartridge is used, presumably, to accommodate larger sample volumes to retain the more highly polar compounds such as metformin. However, much smaller cartridges have been used successfully and should be allowed, particularly if quantification of the most polar compounds is not needed.

- The extraction procedure described in the EPA method is actually two separate extractions (acid/neutral and basic) using two cartridges and two one-liter samples. Some laboratories have found that a single acid/neutral extraction is sufficient if quantification of Cimetidine, Aluterol, ranitidine, and metformin is not needed. Although the described modifications to the EPA method's extraction procedures will result in the inability to quantify some compounds, it is likely to produce more accurate and reproducible results for other, possibly more relevant compounds.

- The 1694 method analysis includes four individual analytical runs using three columns and six solvents. This method has been successfully modified and validated for some compounds using only two analytical runs, two columns and three solvents.

- The 1694 method also specifies that a 15 µl injection volume be used. Such large injection volumes can provide improvements in the sensitivity of the LC/MS/MS system but are also likely to result in matrix suppression problems in more complex matrices. Some laboratories have been able to demonstrate acceptable performance with injection volumes of 2 µl.

- The use of internal standards is essential with the use of isotopic labeled standards (13C, 15N or deuterium) being most accurate. However, labeled standards are extremely expensive ($100 to $5000 per 0.1 mg). In general, matching internal standards with specific analytes is extremely challenging and individual laboratories have developed various programs using labeled and unlabelled standards that combine acceptable laboratory performance with cost considerations. In some instances, the use of labeled standards with only a few labeled molecules for some larger analytes has been demonstrated to be unreliable and successful use at one laboratory may not be demonstrated at another. For example, EPA has neglected using some very reliable labeled compounds, such as carbamazepine d10, that have been successfully used by the other laboratories.

  The internal standards could conceivably be modified and still be capable of assessing IPR acceptance. Changing the labeled analogs would make it difficult to assess the IPR, however additional labeled analogs would be acceptable. EPA should make some allowance for substituting labeled analogs.

- The method only uses one multiple reaction monitoring (MRM) transition. There should be at least two MRM transitions to allow for positive confirmation of the presence of the analyte.

- Currently, commercial labs are charging approximately $1500 per sample for the full list of analytes

and regulators need to know that costs can be reduced significantly if a smaller number of compounds are desired.

Section 1.6 of the method states that the method is performance-based, which does provide for some flexibility, allowing for modification to address some of our concerns above. In fact, the method has been successfully modified at several laboratories resulting in improved performance for selected analytes. Nevertheless, the extent of allowable modification is limited (40 CFR Part 136.6 states that the determinative method cannot be changed), and any modifications to make the method less onerous would require a level of sophistication that some small labs may not have.

Method 1698

NACWA believes that the poor quality control and single laboratory validation results associated with EPA Method 1698 makes the method unacceptable for use in a regulatory context. In addition, the required use of high resolution GC/MS instrumentation combined with the lack of acceptable performance in even "clean" reagent water samples significantly limits this method's utility for use for general water quality monitoring of final effluent and receiving water to address specific public concerns. Method 1698 may provide some useful information for general experimental testing of highly complex samples such as influent and biosolids but the lack of acceptable performance on even "clean" samples and its reliance on high resolution GC/MS instrumentation and complex extraction /clean-up procedures significantly limits the methods utility. Specifically:

- The analytical procedures contained in the EPA 1698 Method require quantification using high resolution GC/MS. This instrumentation is expensive and not widely available to most laboratories.

- Specified extraction procedures (liquid/liquid) may be inefficient in terms of costs, time, and wastes generated compared to solid phase extractions.

- Extracted samples require labor-intensive clean up procedures using packed alumina/florisil columns, presumably to obtain suitable samples for analyses when analyzing "dirty" samples such as influent and solids.

- Reagent water recoveries for some compounds were unsatisfactory with average recoveries as low as 23% and as high as 275% for selected compounds.

Considering that this method requires the use of uncommon and expensive instrumentation, complex extraction and clean up procedures, and single laboratory reagent water recoveries were unacceptable (recoveries less than 70% or greater than 130%) for twenty-five of the thirty-seven analytes evaluated, the method would seem inappropriate for use as a nation-wide monitoring tool.

Currently reported quality control criteria in the method lists ongoing precision and recovery standards (OPR/LCS) of 5% to 200% for eight compounds including progesterone with upper limits of over 180% for seventeen of the twenty-seven compounds evaluated (Table 5 on page 57). Several laboratories have successfully developed steroid quantification methods for a subset of the analytes utilizing more commonly available instrumentation with less complex extraction and clean-up procedures for water samples in relatively clean matrices such as surface waters and final effluents. Jose Creek Water Quality Laboratory (Sanitation Districts of Los Angeles County, Whittier, CA) has validated single laboratory recoveries for estrone, 17a-ethinylestradiol, and progesterone ranging from 98.6% to 104% with quality control standards (OPR/LCS) ranging from 70% to 130%.

Other laboratories are also reporting similar improvements utilizing less expensive and more readily available instrumentation and techniques for steroids as well (Southern Nevada Water Authority, U.S. Geologic Survey).