paper for other materials, including petroleum products and petroleum process catalysts.

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Exchange of Comments: Analysis of Complex Volatile Mixtures by a Combined Gas Chromatography–Mass Spectrometry–Computer System

Sir: We are writing to correct several errors in the paper of Gates et al. (*1*) concerning previously published results from our laboratory (*2, 3*). In a detailed discussion of our work in the above paper, the authors seek to compare our methods with their own. During the course of this discussion, and in other places in their otherwise excellent paper, erroneous statements are made which in our judgment reflect badly on both laboratories and will result in considerable confusion in the minds of readers of the paper.

First, a very important comparison is never explicitly stated in their paper. Their system (*1*) is designed specifically to quantitate previously observed compounds and is applicable to mixtures where the only interest is quantitation of these constituents. Our efforts (*2, 3*) have been directed toward the more general problem of detecting and quantitating both previously observed and new compounds. Both methods have their advantages and disadvantages. These are confused, however, by the discussions of Gates et al. (*1*).

Second, we wish to correct the following specific points:

(1) None of our methods utilize reverse library search (*1*, p 439 and p 440). The HISLIB (*3*) program utilizes "forward" library search and comparison in all phases of operation.

(2) The CLEANUP (*2*) program applies its doublet resolver recursively to deconvolute multiplets (*2*, p 1372). Although one might criticize this approximation, the program is not now, nor has it ever been, limited to simple doublets (*1*, p 437 and

p 440) and routinely handles complex multiplets with limitations similar to those discussed by Gates et al. for their own procedures.

(3) Our work makes explicit use of internal standards (*3*, p 1623 (abstract) and throughout the remainder of paper), not external standards as alleged (*1*, p 440).

(4) Although we have not published data on the accuracy, sensitivity, and linear range of our methods, we have published data on its precision (*3*).

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Sir: In a recent paper (*1*) we made erroneous statements about the techniques developed at Stanford University (*2, 3*) for the analysis of complex volatile mixtures by a combined gas chromatography–mass spectrometry–computer system. As Rindfleisch, Smith, and Yeager have indicated above, the HISLIB program (*3*) uses "forward" library search algorithms rather than "reverse" library search and quantitation is based on internal standards (*3*), not external standards. Furthermore, Smith et al. (*3*) have reported percentage standard deviation of their procedure in the analysis of relative concentrations of reference hydrocarbons and of urinary organic acids obtained either by organic solvent extraction or by anion-exchange chromatography. We regret that these errors have appeared in our discussion of the Stanford system, which is an alternative approach to our MSSMET system for quantitative metabolic profiling. It does have several important advantages that are not yet implemented in MSSMET, including detection and quantitation of previously unobserved (novel) compounds. We certainly did not intend to denigrate the excellent work (*2, 3*) by this group.

The objection by Rindfleisch, Smith, and Yeager about the capability of their CLEANUP program (*2*) to deconvolute multiplets needs to be clarified. Our opinion, after having read their paper (*2*), was that several points were not clearly presented and documentation was minimal. In retrospect, we should not have said (1) that "their system can resolve doublets but not multiple overlapped mixtures of substances" because it was explicitly stated (*2*, p 1372) that sequential use of the doublet resolver can be used for the multiplet case. They go on to point out, however, that the full procedure has not been implemented beyond the doublet case (*2*, p 1372), and that the procedure may not perform very well with complex multiplets, in terms of producing accurate amplitude information (*2*, p 1374). We interpreted these statements to mean that they were not running the system routinely on complex multiplets and had not yet documented a capability to deal with such mixtures effectively. The analysis of multiplets by MSSMET depends on the choice of a single, *unique* designate ion, rather than a cleaned-up spectrum, for each substance in the multiplet and has, indeed, been shown