

## CORRESPONDENCE

study by McEwan and colleagues<sup>2</sup> was 1.23%. An inspired concentration of 70% nitrous oxide should therefore be equivalent to  $0.63 \times 1.23 = 0.77\%$  end-tidal isoflurane in terms of its contribution to MAC. Inspection of figure 3 (which plots isoflurane MAC against plasma fentanyl concentration) of McEwan *et al.*'s study shows that the plasma fentanyl concentration required to produce a reduction in isoflurane MAC to 0.77% is approximately 0.9 ng/ml (95% confidence interval 0.5–1.3 ng/ml). This contrasts dramatically with the minimal steady-state plasma fentanyl concentration of 3.26 ng/ml for achieving the same patient response end-point (and equivalent anesthetic "depth") in conjunction with 70% (0.63 MAC) nitrous oxide. This difference lies well beyond the 95% confidence interval limits quoted for the plasma fentanyl concentration. This implies either that the interactions between nitrous oxide and fentanyl and between isoflurane and fentanyl in generating a 50% suppression of response to surgical incision are dramatically different, or that sub-MAC fractions of nitrous oxide and isoflurane are in fact not equivalent.

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*In Reply:*—Using a MAC value for nitrous oxide of 105% and assuming that the interaction of nitrous oxide with isoflurane is simply additive, it appears that the potency of fentanyl does vary according to whether it is combined with nitrous oxide or isoflurane.

It recently has been demonstrated that the nitrous oxide MAC in rats is greater than that previously reported. Gonsowski and Eger have shown that the MAC in several strains of rats is almost 50% higher than that previously reported.<sup>1</sup> Although that study involved rats, it may be hypothesized that the values extrapolated to humans also are much greater than previously thought. Schwilden and Ropcke have reported on the interaction between isoflurane and nitrous oxide in suppressing the electroencephalogram signal.<sup>2</sup> Extrapolation of their data also supports a nitrous oxide MAC value greater than 105%. Thus, the actual MAC contribution of 67% nitrous oxide may well be much less than 0.63 MAC, thereby explaining the difference in the potency of fentanyl when it is combined with nitrous oxide or isoflurane. Another explanation for the difference in the potency of fentanyl with nitrous oxide and isoflurane is that the interaction between nitrous oxide and isoflurane for MAC determinations is not simply additive. This is supported by two recent publications that have shown that the interaction between nitrous oxide and isoflurane, again in rats, in providing 1 MAC is not linear.<sup>3,4</sup> If this interaction is not linear, then the simple calculations done by Sanders no longer hold.

It is our contention that the potency of fentanyl is not altered by the anesthetic with which it is combined, but rather that the expla-

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nations above are responsible for the apparent discrepancy suggested by Sanders.

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