though their incidence was statistically insignificant. The use of Fischer rats in these studies may have resulted in an underestimate of the carcinogenic effects of phenacetin, since Fischer rats are known to be relatively resistant to the induction of extrahepatic tumors by aromatic amines (4). In contrast, aromatic amines may induce high incidences of mammary and ear duct tumors in Sprague-Dawley rats (5). Such tumors were found by Johansson and Angervall in their 1976 phenacetin study (2).

The claims made by Macklin et al. concerning the use of pelleted diets are speculative. Much of their argument is based on the premise that the melting point of phenacetin is exceeded in the pelleting process. The melting point (mp) of phenacetin given in their letter is incorrect; phenacetin melts at 134° to 135°C (6) (273° to 275°F), not at 134° to 135°F. Even if the melting point were reached, they present no evidence that significant degradation would occur or that N-oxidation would occur spontaneously.

The argument that the Charles River Formula diet used by Isaka et al. (2) contains N-nitroso derivatives which might be responsible for tumorigenicity overlooks the fact that control animals fed the same formula developed only a small number of tumors. Whether there may be synergistic effects between nitrosamines in commercial feed and test compounds is a matter of some concern (News and Comment, 13 Oct. 1978, p. 192; Letters, 8 Dec. 1978, p. 1034; Letters, 5 Jan., p. 7) that has not been resolved. While there is no evidence that this phenomenon occurred in this instance, phenacetin can act synergistically with at least one carcinogenic nitrosamine in the induction of urinary bladder tumors (7). To minimize this carcinogenic effect of phenacetin would ignore the cumulative effects of the exposure of humans to a multiplicity of carcinogens over their lifetime.

Although the structure of phenacetin allows for a number of metabolic reactions that are not possible with 2-acetylaminofluorene, N-hydroxylation of phenacetin does occur, and there is reason to believe that this is a vitally important step in the metabolic activation of phenacetin, as it is for 2-acetylaminofluorene (8). N-Hydroxyphenacetin is both a carcinogen (9) and, when enzymatically activated, a mutagen (10). The possibility that phenacetin may be nitrosated has received little attention (11).

In contrast to the claim by Macklin et al., both phenacetin and N-hydroxyphenacetin have been demonstrated to be mutagenic to Salmonella typhimurium TA 100, with the supernatant (9000g) from hamster liver homogenate as the activating system (12).

Although phenacetin is not as potent a carcinogen as some others to which we are exposed daily, we believe that its use in nonprescription analgesics should be banned. The ever-increasing body of data from animal and human studies concerning the metabolism, mutagenicity, and carcinogenicity of phenacetin, is impossible to ignore. Swedish and Australian authorities have long since taken action to minimize exposure to phenacetin. The documented cumulative effects of carcinogens argues strongly for the reduction of exposure to phenacetin. Alternative analgesics are available.

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Erratum: In the report by M. E. Trulson and B. L Lacobs, "Long-term amphetamine treatment de-creases brain serotonin metabolism: Implications for theories of schizophrenia" (21 Sept., p. 1295), the column headings "Norepinephrine" and "Trypto-phan" in Table 1 (p. 1296) are transposed. The data under "Norepinephrine" should have been listed under "Tryptophan," and vice versa. Errotum A News and Comment briefing "Car-

under "Tryptopnan, and vice versa. Erratum. A News and Comment briefing, "Car-cinogens in Scotch" (24 Aug., p. 769), incorrectly re-ported that carrot and beet juice contain relatively high levels of nitrosamines. So far as is known, they do not. They do contain nitrates and nitrites, the precursors of nitrosamines.

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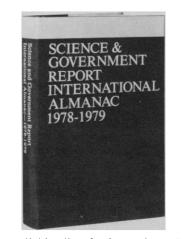
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