Approval of New Drugs

In his report on drug regulation (News and Comment, 23 Feb., p. 777), Nicholas Wade says that the Food and Drug Administration (FDA) was saved "from having to answer on possibly embarrassing points of detail" because my paper is unpublished, but that its answer to "the general thesis" was "quite effective." This comment deserves a reply.

First, the ground rules for the FDA's answer were their own; they have had copies of my paper since late last year. More important, the "embarrassing points of detail" include every substantive point of my analysis. It was not my purpose to malign the FDA for perversely holding good drugs from the market, or to claim that the 1962 Kefauver amendments have never benefited consumers. Thus, much of the FDA's testimony was irrelevant. I attempted an *overall* assessment of the working of the 1962 amendments, and my finding that, taken as a whole, the amendments have produced fewer benefits than costs was never rebutted by the FDA. Specifically, among the results of my research that still await rebuttal are:

1) The pre-1962 decline in drug innovation has a perfectly sensible economic explanation (a decline in drug market growth in the mid-1950's) that fails to rationalize the low post-1962 innovation rate.

2) The decline in innovation since 1962 has been too substantial to attribute all or even any great part of it to preemption of ineffective drugs. Many effective drugs are not marketed, not because the FDA is perverse, but because the cost burden of the amendments on the process of drug development makes their development unprofitable.

3) When conservative estimates of the value forgone because potentially effective drugs are not developed is set off against estimates of the consumer savings attributable to the amendments, the net balance is decidedly unfavorable to the consumer.

4) The probable costs of delayed introduction of unusually effective drugs, an inevitable result of the added testing required to satisfy the amendments, exceed manyfold a generous estimate of the value of improved drug safety that the amendments are likely to produce.

These points cannot be rebutted by simple extrapolation of trends, selected examples of the FDA's competence, or contrary assertions. Quite apart from the shortcomings of the FDA's testimony, I regret that the FDA chose to view my research as a specific critique of that agency. The FDA happens to be the instrument Congress chose for administering the amendments. However, the inherent defect is in Congress's mandate to the FDA, and it would be unreasonable to look to the FDA rather than to Congress for repair of that defect.

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Nicholas Wade quotes Henry E. Simmons as stating that every year, between 3 and 5 percent of those hospitalized, or 1.5 million people, are admitted primarily because of drug reactions. Strongly implicated as causes are the risky nature of prescription drugs and the lack of skill and discrimination in their use by physicians.

These ominous figures are shocking and hard to believe, as no doubt they were intended to be. However, serious inflation has occurred between the original work and final citation.

The Simmons data derive from a review paper by K. L. Melmon (1), who cites five research studies to substantiate his figures (2–5). The first of these, the work of Seidl et al. at the Johns Hopkins Hospital, has been cited elsewhere (7) as the basis for a national projection of 1.5 million drug-caused admissions. Seidl et al. had reported that 5 percent of patients were admitted with a drug reaction; a later study by the same group showed 1.7 percent of admissions because of a drug reaction (8).

In the Johns Hopkins studies (2, 8), these percentages represent admissions to medical wards. Since 20 percent of admissions to Johns Hopkins are to medical services, about 0.4 percent of all patients are admitted to that hospital primarily because of drug reactions. It is unlikely that the experience of a major teaching hospital and referral center like Johns Hopkins can be extrapolated to all hospitals. But doing so would give a figure closer to 150,000 than 1.5 million. The inflationary factor thus appears to be at least 10.

There are similar problems with Simmons' claim that "once in hospital, between 18 and 30 percent of all patients have a drug reaction." Melmon cites two sources for such an estimate: Seidl et al. (2) report that 13 percent had drug reactions while hospitalized to which Melmon adds the 5 percent with reactions present on admission to get 18 percent. Hoddinott et al. (3) report that 15 percent of patients had probable drug reactions to which Melmon adds another 15 percent with forgotten doses and other errors in drug administration to get 30 percent.

Again, both these studies were done on medical wards. It is as wrong to say that 13 or 15 percent of all hospitalized patients have a drug reaction (although this may be true for one ward) as it would be to say that 100 percent of all hospital patients are pregnant, because this may be true for one ward. Perhaps it is more important to note that no reaction-incidence study has yet screened out those minor symptoms which are known to occur as "adverse nondrug reactions" (9) in people who take no medication. A placebo-controlled study might yield more realistic figures.

The source material also fails to support the estimate that, for patients with drug reactions, "the length of their stay is about doubled as a result." The authors cited by Melmon to back up this claim (2–5) all agree that there is a positive correlation between length of hospital stay and number of drug reactions observed; but all also agree that very likely "the long hospital stay was the factor predisposing to the occurrence of adverse episodes" (4) and not the other way around.

Finally, these excessive estimates tend to link the adverse reaction problem with the introduction of new drugs. Actually, surveys of drug reactions show that it is the older drugs, such as quinidine, digitalis, and insulin, used in medical practice for over 30 years, which are most often found at fault (5). Advances in drug technology may thus help reduce the real incidence of undesired side effects from medical treatment.

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Another Scientist in Congress

Constance Holden (News and Comment, 18 May, p. 720) writes that there is only one scientist in Congress—Mike McCormack (D–Wash.). Another scientist in Congress is James G. Martin (R–N.C.), who was, until his election to the House of Representatives last fall, associate professor of chemistry at Davidson College.

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Taxation and Energy Conservation

The letter from P. de Haen concerning conservation of gasoline (13 Apr., p. 137) deserves comment. European governments tax automobiles on the basis of taxable horsepower, which is a meaningless number calculated from