An Evaluation of Consumer Protection Legislation: The 1962 Drug Amendments

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The 1962 drug amendments seek to prevent wasted expenditure stimulated by exaggerated claims for effectiveness of new drugs by requiring premarketing approval of all new drug claims by the Food and Drug Administration. The compliance costs are shown to have engendered a marked reduction in drug innovation. Consumer surplus analysis is then adapted and supplemented with "expert" drug evaluations to estimate the relevant benefits and costs. The main finding is that benefits forgone on effective new drugs exceed greatly the waste avoided on ineffective drugs. The estimated net impact is equivalent to a 5–10 percent tax on drug purchases.

I. Introduction

The 1962 Kefauver-Harris Amendments to the Food, Drug, and Cosmetics Act are a landmark of the modern consumer movement. While they continued a tradition of legislative attempts to improve product safety, their primary aim of preventing economic loss by regulation of product quality still has few counterparts.

The initial impetus to the 1962 amendments came from hearings begun in 1959 by Senator Kefauver's Antitrust and Monopoly Subcommittee. A major theme developed there was that many new drugs of dubious efficacy were being marketed at unusually high prices. New chemical formulas qualify for patent protection, and information about

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them had to be obtained by most physicians outside their formal training in pharmacology. The only legal restriction then placed on the marketing of new drugs was that the Food and Drug Administration (FDA) could, within a statutory maximum period of 180 days, deny approval of a new drug application (NDA) and thereby prevent sale of a new drug if the NDA did not adequately demonstrate that the drug was "safe" for use as suggested in proposed labeling. It was alleged in the Kefauver hearings that these circumstances provided powerful incentives for drug companies to develop minor variants of existing drugs and capitalize on their patent protection with expensive promotion in which exaggerated claims of the new drugs' effectiveness would be impressed upon physicians (and, sometimes, their patients). Physicians, in part because they did not directly bear the cost of the drugs, would treat these claims with insufficient skepticism. The resulting demand for the new drugs would thus be sufficiently large for sellers to more than recoup their promotion and development expenses, and the net result would be that patients paid far more than the true worth of the new drugs. This view of the drug market was summarized well at the Kefauver hearings by a former drug-company medical director:

> . . . industry spokesmen would have us believe that all research is on wonder drugs or better medicinal products. They stress that there are many failures for each successful drug. This is true . . . . The problem arises out of the fact that they market so many of their failures . . . . Most [industries] must depend on selling only their successes . . . . [But] with a little luck, proper timing, and a good promotion program a bag of asafetida with a unique chemical side chain can be made to look like a wonder drug. The illusion may not last, but it frequently lasts long enough. By the time the doctor learns what the company knew at the beginning it has two new products to take the place of the old one. [U.S., Congress, Senate, Judiciary Committee 1961, p. 127; see also chaps. 6–15]

Senator Kefauver concluded that government regulation of manufacturer claims for new drug effectiveness would be a cheaper source of information about new drugs than hindsight. It is, however, doubtful (see Harris 1964) that such regulation would have been enacted without the intervention of the thalidomide episode of 1961 and 1962. Thalidomide was, in fact, kept from the U.S. market by the FDA under the then-existing law, but the drug had been distributed to some physicians for experimental purposes. Such distribution was lightly regulated, and reports of births of deformed babies to European mothers who had taken the drug raised concern here that, in their rush to market new drugs, manufacturers were egregiously exposing humans to potentially harmful

drugs during clinical testing. This concern served as a catalyst for the enactment of the 1962 drug amendments.

This paper focuses on the provisions of the amendments related to new drugs, and only the most important of these are summarized here:

1. A "proof-of-efficacy" requirement was added to the existing proof-of-safety requirement, and the time constraint on FDA disposition of NDAs was removed. This meant that no new drug could be marketed unless and until the FDA determined that the drug was both safe and "effective" in its intended use. In this context, an effective drug is one which the FDA determines will meet the claims made for it by the manufacturer. In its promotion of the drug, the seller can claim only those effects established before the FDA, and the promotion must include a summary of "side effects, contraindictions and effectiveness."

2. The testing procedure a manufacturer employed to produce information for an NDA was made subject to FDA regulation. Under this regulation, a manufacturer must submit a plan for any clinical tests to the FDA along with information from preclinical tests. The FDA may, at any point, terminate or order changes in the clinical investigation if the drug is deemed unsafe or ineffective.

These provisions were meant to spare ignorant consumers from wasting money on drugs which could not live up to exaggerated claims, first, by subjecting the claims to premarket evaluation by the FDA and, second, by assuring that the FDA could have sufficient information to make the evaluation. This system of premarket evaluation and regulation of clinical testing would also, it was hoped, reduce human exposure to drugs like thalidomide before and after marketing.

This paper seeks to determine whether, and to what degree, consumers have succeeded in obtaining a more valuable flow of new drugs under the regulatory system engendered by the 1962 amendments. Their specific effects on drug safety are not treated here. (See Peltzman [in press] for a fuller discussion of drug safety.) I begin by estimating the effects of the amendments on the sheer size of this flow. If the amendments are more than well-intentioned verbiage, they could be expected to have reduced the flow of new drugs directly (eliminating those deemed ineffective by the FDA but not by the manufacturer) and indirectly (through reaction to costs associated with the expanded information requirements of the amendments). While I show in the next section that the amendments have indeed substantially reduced the flow of new drugs, this only focuses the question of their effects on consumer welfare more sharply. A large reduction in the flow of new drugs, unless it is offset by increased consumption per new drug, can be consistent with large net benefits or large net costs, depending on the magnitude of the preamendment cost of ineffective drugs and the selectivity with which the amendments operate against ineffective drugs. Section III shows how

consumer surplus analysis can be adapted to measure the relevant benefits and costs; Section IV carries out the estimation and then checks the results against some "expert" drug evaluations. The principle conclusion is that the amendments have generated substantial net costs for consumers, and the conclusion is not altered if "expert" judgment is substituted for that of the marketplace.

II. Introduction of New Drugs

A glance at table 1 indicates that there has been a precipitous decline in the flow of new drugs since 1962. The post-1962 flow is less than half that prior to 1962, and there was no obvious downward trend prior to 1962. However, I want to allow for the possibility that some, all, or even more than all[1] of this decline was due to fundamental change, unrelated to the amendments, in factors underlying the demand or supply of new drugs. Therefore, I first develop a model for the "unregulated" introduction of new drugs, and then estimate its parameters on pre-1962 data. These parameter estimates are then used to project post-1962 drug flows. A comparison of these projections with actual post-1962 flows provides an estimate of the effects of the amendments.

My model treats each drug formula as a homogeneous bit of nondepreciable therapeutic information. I assume that the demand for these bits by drug producers is derived from the expected size of the drug market. Specifically,

$$N_t^* = f(X_t^*), \tag{1}$$

where N_t^* = number of drug formulas producers wish to have available for marketing in year t and X_t^* = output of drugs producers anticipate in year t. Producers must anticipate the size of the drug market, because production of new drugs entails a lengthy research-and-development process. I assume that these anticipations are based on naïve extrapolation of current levels of drug output and current output of an important complement, physicians' services. That is, if drug producers observe, say, a decline in output of drugs or a decline in output of physicians' services, they will revise downward their estimate of future drug output and reduce the resources committed to the new-drug development process.

[1] That is, it might be argued that the 1962 amendments were in the nature of a "public good" for the drug industry which could have raised the demand for new drugs. If many ineffective drugs were being marketed prior to 1962, there would have been a large demand for independent evaluation and certification of new drugs. However, costs of detecting and excluding free riders may have deterred direct sale to consumers of such evaluations by a private producer, while their sale to drug companies may have engendered skepticism which would reduce their value. If the resultant private underproduction of new drug evaluations is corrected by the amendments, the demand price of new drugs would be increased more than the costs of complying with the amendments, and new-drug output would rise.

TABLE 1
AVERAGE ANNUAL NUMBER OF NEW DRUGS INTRODUCED, 1951–70, SELECTED SUBPERIODS

Period	New Chemical Entities	Other New Drugs
1951–54	39.0	303.0
1955–58	42.0	351.5
1959–62	43.5	239.3
1963–66	17.0	120.0
1967–70	15.3	68.8
1951–62	41.5	297.9
1963–70	16.1	94.4
Ratio (1963–70/1951–62)	0.389	0.317

SOURCE.—Paul de Haen, Inc., New York.
NOTE.—"New chemical entities" are drugs containing a single chemical formula not previously marketed. "Other new drugs" are new combinations of previously marketed chemical entities and duplicates of chemical entities marketed under a new brand name (usually by a new manufacturer, sometimes for a new therapeutic indication). About 80 percent of "other new drugs" are combinations. Data on new dosage forms, e.g., a tablet form of a liquid, are omitted. Their flow has paralleled that of other new drugs, falling from 104.5 per year in 1951–62 to 26.4 annually for 1963–70.

This reduced R & D commitment then translates into a reduced N^* in the future. This may be expressed:

$$X_t^* = g(X_{t-j}, P_{t-j}), \tag{2}$$

and, from (1),

$$N_t^* = h(X_{t-j}, P_{t-j}), \tag{3}$$

where P = output of physicians' services and j = gestation period for a new drug.

One would expect the cost of producing drug formulas, as well as their demand, to affect N^*. For example, since much of this cost is labor expense for R & D personnel, the relative wage of R & D to production personnel ought to influence the extent to which changes in X^* are met from existing or new drug formulas. Unfortunately, construction of an empirical counterpart to this relative wage variable is precluded by lack of continuous data on wages of R & D personnel, so the variable is omitted here. However, based on fragmentary data, this omission will not seriously bias the subsequent estimate of the effects of the 1962 amendments. There is no apparent upward trend or post-1962 increase in the relative wages of R & D and production personnel.[2]

[2] The Bureau of Labor Statistics (BLS, *b*) reports that, from 1961 to 1970, the average annual salary of chemists (a prototypical form of research labor) rose by 50.2 percent. This corresponds closely to the 52.6 percent rise in average hourly earnings of drug-industry production workers (BLS, *a*). Data from the U.S., Bureau of the Census, *Census of Population* show that, from 1949 to 1959, median annual income of chemists rose by 63.8 percent while that of "natural scientists" rose 74.0 percent. In the same period, BLS data show a 55.8 percent increase in drug-production worker average hourly earnings (BLS, *a*). Taken together, then, the data imply a slightly more favorable labor-cost environment for research after 1962 than before. However, annual earnings of research personnel could have been unduly depressed by the 1949 recession, and the safest conclusion would be that no obvious labor-cost inducement to substitute production for research activity can explain any of the post-1962 decline in new drug innovation.

It remains then for us to specify how producers react to the demand for drug formulas in supplying *new* formulas in any marketing period (1 year). The annual flow of new drugs may, in this context, be regarded as an attempt by producers to close the gap between the number of formulas they wish to have on the market and those already developed and marketed. I assume that the cost of closing this gap will rise with the rate at which it is closed, so that producers may not wish to eliminate the gap entirely in one marketing period. If this adjustment process is linear, we may then write:

$$n_t^* = k(N_t^* - N_{t-1}), \tag{4}$$

where n^* = number of *new* drug formulas producers wish to market, N_{t-1} = number of formulas available for marketing at the start of year t, and k = a constant coefficient of adjustment between zero and unity.

To implement (4), I assume that producers attain n^* on average, with deviations being random. I also assume that (3) is linear in form, so that when its right-hand side is substituted for N^* in (4) we get

$$n_t = a + bX_{t-j} + cP_{t-j} - kN_{t-1} + u, \tag{4'}$$

where a, b, c = constants and u = random variable.

The empirical counterpart to the dependent variable will be new chemical entities (NCEs), that is, single chemical formulas not previously marketed (as opposed, e.g., to new combinations of existing formulas). The motivation for this focus will become clear subsequently. Suffice it to say here that NCEs include almost all important therapeutic breakthroughs and have triple the development expense of a combination product (Schnee 1970, p. 77). I use Schnee's (1970, p. 77) estimate that mean development time of a (pre-1962) NCE was about 2 years with standard deviation of 1 year in constructing empirical counterparts to X_{t-j} and P_{t-j}.[3] To conserve degrees of freedom, these counterparts employ three-term moving averages centered about $t - 2$.

The least-squares estimate (E = estimate) of (4') on pre-1962 data is:

$$n_t = -2990.016 + \underset{(75.616)}{471.352}\bar{X}_{t-2} + \underset{(32.142)}{45.590}\bar{P}_{t-2} - \underset{(.113)}{.672}N_{t-1}, \tag{E1}$$

where coefficient of determination = .800; standard error of estimate = 4.969; sample period is 1948–62 (15 observations); standard errors of coefficients are in parentheses; n_t = number of NCEs introduced in t (data provided by Paul de Haen, Inc., New York); $\bar{X}_{t-2}$ = log of 3-year moving average of total number of out-of-hospital prescriptions sold (millions) centered about $t - 2$ (*American Druggist*); $\bar{P}_{t-2}$ = log of 3-

[3] Development time comprehends the period from clinical testing of a chemical entity with desirable biological activity to approval of an NDA.

year moving average of personal consumption expenditures on physicians' services (million dollars) deflated by price index (1958 = 100) for these services and centered about $t - 2$ (U.S., Office of Business Economics 1966*a*, 1966*b*); and N_{t-1} = cumulative number of NCEs introduced through $t - 1$ (Paul de Haen, Inc., New York).[4] The regression implies that size of the drug market is by far the more important of the two demand variables[5] and that roughly two-thirds of the gap between N^* and N is closed in any annual marketing period. This rather simple model is, given the size of the coefficient of determination, able to explain most of the variation in NCE flows in the postwar period up to 1962. The satisfactory performance of the model is confirmed by inspection of figure 1, where actual values of n are plotted against the values predicted by (E1). There were at least two major cycles (beginning 1948 and 1955) in NCE flows in the pre-1962 period, and the model "tracks" both of them closely. It is especially important, in light of post-1962 experience, to note that the decline from the postwar peak (63 NCEs in 1959) to the trough (27) just prior to passage of the 1962 amendments is virtually all accounted for by the variables in (E1).

We next use (E1) to predict annual NCE flows in the post-1962 period and compare these predictions with actual flows. The predicted flows are estimated by plugging post-1962 values of $\bar{X}$ and $\bar{P}$, along with the implied values of N, into (E1);[6] they may be regarded as estimates of n in the absence of any change in the law. These estimates are also plotted in figure 1, and they imply that, but for the 1962 amendments, there would have been a gradual recovery in NCE introductions from the 1962 trough to a level in excess of 40 per year for most of the 1960s. Although the model predicts that post-1962 NCE flows would not have attained the peak pre-1962 levels, the average post-1962 predicted flow is 41 per year which is virtually identical with the average pre-1962 flow (40). The mean difference between the predicted and actual post-1962 annual flows (25) is over 10 times its standard error and only in the transition year, 1963, is the difference much smaller (15) than this average. I conclude from these data that (*a*) the 1962 amendments significantly reduced the flow of NCEs and, what is perhaps more interesting, (*b*) *all* of the observed difference between pre- and post-1962 NCE flows can

[4] The cumulation is begun from 1945, so that N_{t-1} is, in fact, the "true" number of chemical entities developed to $t - 1$ minus a constant (the number developed to 1945). This difference between N_{t-1} and the "true" value will affect only the intercept of the regression estimate of equation (4′). The cumulation procedure assumes no "depreciation" of the stock of chemical entities. In fact, old chemical entities are sometimes withdrawn from the market, but this does not imply that the knowledge embodied in them has "worn out." That knowledge is nondepreciable, and so we treat each NCE as a net addition to the stock of knowledge.

[5] A given percentage change in X increases the demand for chemical entities by more than 10 times that of the same percentage change in P.

[6] That is, N is computed by adding the post-1962 predicted values of n to N_{1962}.

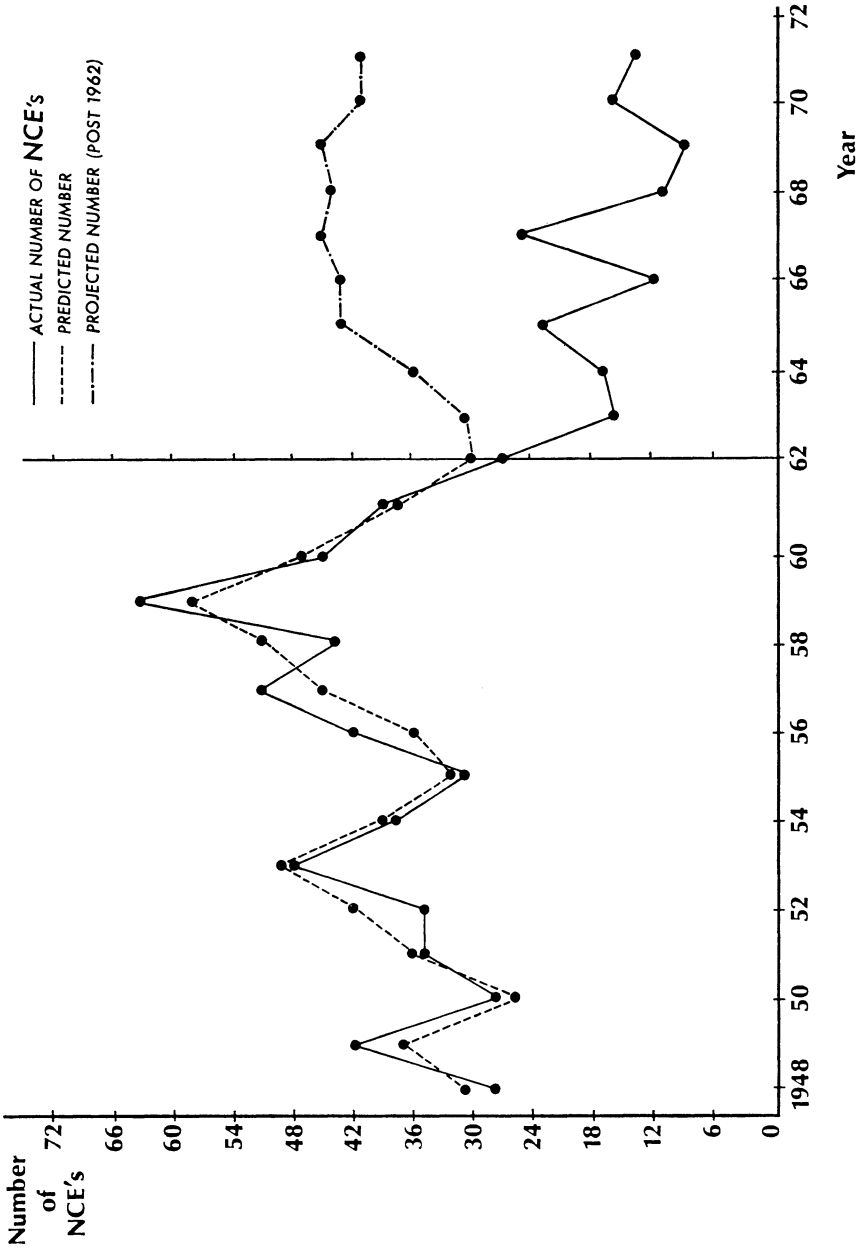

FIG. 1.—New chemical entities, 1948–71

be attributed to the 1962 amendments.[7] While this conclusion appears strong, it tends to be supported by a simple comparison of U.S. and British NCE flows. Data reported by Wardell (1972) show that, for 1960–61, the U.S. flow was 1.13 times the British, while, for 1966–71, this ratio was only 0.52, or 0.46 of its pre-1962 value. This last figure is already roughly comparable in magnitude to the ratio of U.S. NCEs to the number predicted by (E1) for 1966–71 (0.34). However, simple enumeration of British post-1962 NCE flows probably understates the amount of innovation to be expected in a pre-1962 regulatory environment and, correspondingly, understates the effect of the amendments in the United States. Most of the British NCEs are produced by firms with substantial sales in the United States, and the British NCE flow is reduced whenever the cost of complying with the U.S. law is sufficiently great to deter development of an NCE for both markets. While a detailed study of this transnational effect of the amendments is beyond the scope of this paper, the simple comparison of American and British experience lends credence to the large effects I have attributed to the amendments.

To the extent that some of the costs of complying with the amendments are "fixed"—that is, unrelated to the size of a new drug's market—one might expect that output of new drugs has declined less than their number. However, there is no strong evidence that drug manufacturers have been successful in achieving larger output per NCE than prior to 1962, though there is some indication that they have tried to do so. In subsequent analysis I use a sample consisting of "important" NCEs. These are NCEs which account for 1 percent or more of prescriptions sold in a submarket which itself typically accounts for over a million new prescriptions annually. Number of prescriptions is, to be sure, a rather crude output measure, and the criteria defining submarkets

[7] To check the reasonableness of these conclusions, I replicated a variant of (4′) on cross-sectional data. The data are for drug submarkets in 1960–62 and will be described more fully later. Because of data limitations it is necessary to assume continuously complete adjustment of N to N^*. Therefore, n is regressed on the change in X for each submarket; the level of X is retained because the larger submarkets should have more NCEs. The regression is

$$n_i = \underset{}{.394} + \underset{(.884)}{1.901}\dot{\bar{X}}_{i,t-2} + \underset{(.098)}{.195}\bar{X}_{i,t-2}, \qquad \text{(E1′)}$$

$R^2 = .14$, $i = 1, 2, \ldots, 42$ submarkets where n_i = average annual number of NCEs in submarket i for 1960–62 and $\dot{\bar{X}}$ = average annual change in $\bar{X}$. I next used (E1′) to extrapolate forward and backward in time on the aggregate data. Since the scale of the dependent variables in (E1) and (E1′) differ, it is convenient to express the results as an index. For 1948–59, (E1′) predicts an average n equal to 109 percent of the 1960–62 average. The actual average using aggregate data is identical to this. For the period 1963–70, the average predicted value for n is 106 percent of the 1960–62 average. The actual value, however, is only 43 percent. Extrapolation from the cross-sectional results, then, leads to the same conclusions as that from the time series: all of the large post-1962 decline in drug innovation must be attributed to extramarket forces, such as the amendments.

(therapeutic categories) may not always correspond to relevant economic criteria. I shall, however, tolerate these imperfections in order to be able to work with disaggregated data.[8] The percentage of all drug prescriptions accounted for by these important NCEs 1 year after introduction fell from 1.58 in the period just prior to the amendments (1960–62) to 0.57 subsequently (1964–69, the transition year 1963 is excluded). This decline roughly parallels that in the number of NCEs introduced, so that each NCE captures about the same share (0.1 percent) of total prescriptions in each period.[9] Manufacturers have, perhaps in response to fixed costs of compliance with the amendments, concentrated innovation on larger submarkets since 1962.[10] An explanation for their failure to achieve thereby an increase in sales per NCE is provided in subsequent analysis of the demand for new drugs.

III. Costs and Benefits of the 1962 Amendments: Analytical Framework

The preceding analysis establishes only that the 1962 amendments have had a substantial effect on the new-drug market, but not whether the amendments have benefited or failed their intended beneficiaries. Some of the 200 or so new drugs that would have been introduced in the absence

[8] The data to be used here are from R. A. Gosselin, Inc., *NPA*. The *NPA* uses a sample of prescriptions filled at a panel of pharmacies to estimate national dollar and prescription sales for each drug sold by prescription. Drugs are grouped by two-, three-, and four-digit therapeutic categories according to chemical similarity (e.g., penicillins) and/or similarity of the symptoms for which the drugs are prescribed (e.g., analgesics). Four-digit categories are employed here. The data are limited to new prescriptions, since the *NPA* began collecting data on refills only after 1962. I exclude from my sample of the *NPA* data those therapeutic categories in which the major innovation (50 percent or more of dollar or prescription sales) took place in a single year during or up to 3 years prior to the period being sampled. The motivation for these exclusions derives from the subsequent analysis of the relative output of new and old drugs. Where a category has, in effect, just been invented, it will not contain a reliable sample of old drugs. The categories remaining in my sample account for about 80 percent of all prescriptions sold in a typical year.

[9] These data, however, exclude two important drug categories (diuretics and oral contraceptives) which were essentially invented just prior to 1960, but where substantial post-1962 innovation took place (see above, n. 8). Their inclusion would bring the post-1962 annual NCE share up to 1.18 percent compared to 1.77 percent for the pre-1962 period. It would be risky, though, to conclude from this last comparison that there is a persistent tendency to increased output per NCE. The effect of these few major innovations is concentrated in the first triplet of the post-1962 years, which implies that they are a "spin-off" of preamendments innovation. The average annual NCE share for 1967–70 is a mere 0.36 percent. More important, perhaps, no wholly new drug category has appeared since 1962 which has produced innovations that now seem capable of duplicating the impact of diuretics and oral contraceptives. The safest conclusion to draw here would be that the decline in number of new drugs has been roughly matched by a decline in their output.

[10] The average submarket penetrated by one or more important NCEs in a post-1962 year accounted for 3.49 percent of all drug prescriptions compared with 1.82 percent before 1962. The difference is significant.

of the amendments may have been "worthwhile," and their potential consumers are made worse off by their unavailability. Others may have been "inefficacious" (or unsafe) and their potential consumers are benefited by their unavailability. I shall attempt here to outline a procedure for determining how these gains and losses, and, thereby, the net impact of the 1962 amendments, can be estimated.

The 1962 amendments will be treated here as an attempt to reduce the costs to the consumer (doctor-patient unit) of obtaining information about new drugs. This treatment leads me to estimate the resulting benefits and costs from evaluations of new drugs manifested in the marketplace by well-informed consumers. I am thus taking at face value the view adumbrated at the Kefauver hearings that the major problem requiring a regulatory solution was the underproduction of reliable consumer information on new drugs. One might wish to view the amendments in a somewhat more paternalistic light, namely, as an attempt simply to substitute "expert" judgment for that of even the best-informed consumer. My conjecture, which I subsequently test, is that differences in judgment between these groups should not be pervasive, because, unlike, say, cigarettes and rich food, there appears to be little room for conflict between experts and most consumers over what the desirable characteristics of new drugs are.

The 1962 amendments seek to reduce the cost of new-drug information to the consumer by substituting FDA-produced information for drug-company promotion and information obtained from actual usage. That is, the NDA today restricts what the drug company may claim, but provides the user with independent assurance about the accuracy of what is claimed. This independent assurance is produced by preventing actual usage until the FDA has what it considers sufficient clinical test evidence to make the assurance valuable. I next outline the circumstances in which this substitution of information would benefit drug consumers.

First, consider a pre-1962 consumer of a drug X that has just been placed on the market. He evaluates the benefits of X in the light of the information available to him (the fact of NDA approval plus information provided by, e.g., the manufacturer). This perceived evaluation is summarized by his demand curve for X, ADM in figure 2. If the consumer is faced with a per unit price of OB, his evaluation leads him to purchase OC units, on which he perceives a net benefit of BDA. Now suppose that, in the light of his initial experience with the drug, the consumer discovers that X was not as valuable as he had originally thought—the manufacturer's claims overstate what he discovers to be the drug's effects. Having discovered the drug's genuine value, he then reduces his demand to $GHEN$. He buys only OF units, and his genuine net surplus is BHG dollars per unit of time. He also discovers that, previously, he wasted

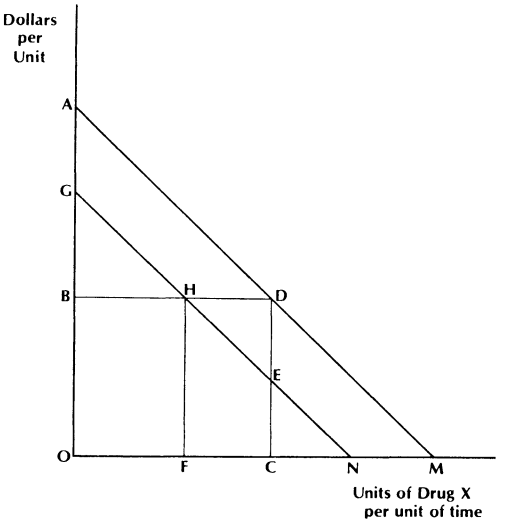

FIG. 2

money. Before he discovered the genuine merits of the drug, he was consuming an extra *FC* units of the drug per unit of time, the true value of which was *HECF*, but for which he paid *HDCF*. These extra *FC* units, therefore, entailed a net loss of *HDE* dollars per period until the consumer learned the drug's true value. Put differently, if an alternative information source had, from the outset, provided the consumer with all the information he obtained by experience, the consumer would have been willing to pay up to *HDE* dollars to this source in each period that he would otherwise have consumed *OC* units. If this source had provided the consumer with this information at a cost less than the value of the stream of his *HDE* losses, the consumer would have been left with a net benefit.

The 1962 amendments established an additional source of information. In this context, the rationale for the amendments would be that, by relying on the information gathering and evaluation expertise of the FDA, the consumer could frequently avoid losses like *HDE*. He may, to be sure, have to pay something for this information, since the costs of the added testing required of drug manufacturers may be reflected in a price above *OB*. This higher price would cause net benefits to be less than *BHG* per unit of time. But, so long as the present value of these reduced benefits fell short of that of his prospective *HDE* losses, the 1962 amendments would yield the consumer a net gain.

The preceding analysis raises important problems if we try to generalize its characterization of the incompletely informed consumer in the pre-1962 environment. Specifically, what consumers have learned about

some new drugs from their market experience should affect their evaluation of other new drugs. If, for example, they find that they have consistently overestimated the benefits of a particular manufacturer's new drugs, their evaluation of claims for his future new drugs will be discounted—the initial and "true" demand curves will come together. We must, however, minimize the empirical importance of this more general learning-from-experience process if we wish to entertain the possibility that the 1962 amendments have conferred net benefits on consumers. Similarly, we must judge empirically unimportant any other private source of information which would reduce quickly the difference between *ADM* and *GHEN*. I shall assume that in the pre-1962 drug market such differences may have been numerous and persistent. I will also treat the pre- and post-1962 drug markets as mutually exclusive and exhaustive states of the world.

To estimate the social gains and losses produced by the 1962 amendments we would want, in this context, to compare estimates of the initial and "true" consumer evaluations of the same new drugs. We cannot, of course, know what both of these are at the time a drug is introduced, since, prior to 1962 at least, the true evaluation depended to a greater extent than now on market experience. Therefore, we shall have to infer this true evaluation from consumer behavior at some time after the drug has been introduced. Further, since we cannot observe evaluations by the same set of consumers of the same drugs marketed under alternative regulatory environments, we will have to compare consumer evaluations of different drugs. This would pose no problem if we could assume that the only important difference between pre- and post-1962 drugs is that the latter have passed through a more extensive review process which unambiguously provides more information. However, the 1962 amendments try to change both the composition and amount of consumer information. Specifically, they regulate the amount of privately produced information which is tied to a new drug. While it is convenient to speak of the consumer as buying pills or prescriptions, he values these for their expected effects on his health. The consumer may wish to spend something to learn these expected effects, and some of this expenditure, most notably that for drug-industry-produced information, will be tied to his purchases of pills and prescriptions. Therefore, the valuations manifested in the market are those for a tied product: pill-*cum*-information. Because the 1962 amendments were designed to change the information component of this package, they may have changed consumer evaluations of the package. Drug manufacturers may no longer advertise effects other than those claimed and certified by the FDA in its approval of an NDA. While this stricture may not prevent all consumption of new drugs for nonsanctioned purposes, it will raise the cost of, and presumably decrease the amount of, privately produced information sold with each new drug.

The amendments may also have reduced the amount of new-drug information unintentionally. Consumers cannot form an evaluation of products of whose existence they are ignorant, and some consumers will learn about a new type of drug when brand A is introduced to them. If the potential seller, faced with the cost and uncertainty of complying with the amendments, never markets brand A, a consumer may remain ignorant about the new drug type, and he will, therefore, not seek out brand B. In this way, the decision not to market A reduces information about and the demand for the new drug type generally. More to the point, perhaps, if neither brand A nor brand B are marketed, the consumer cannot express an evaluation of the drug type, so demand for it will be operationally nonexistent. It was shown previously that essentially all of the drastic post-1962 decline in the number of new drugs can be attributed to the amendments, so this source of reduced new-drug information may well be more important than the explicit restrictions on promotion.

However, the essential motive to the amendments is the possibility that much of this privately produced information may be worthless, so a lower initial demand for new drugs–*cum*–private information following the amendments cannot be interpreted unambiguously. This may be seen with reference to figure 2. Let us suppose that a drug exactly like X is marketed after 1962, but that we observe an initial demand curve for it like *GHEN* instead of *ADM*. This different initial demand could reflect the elimination of exaggerated claims for the drug by the 1962 amendments. It could also reflect the elimination of worthwhile information because manufacturers could not demonstrate the worth of the drug to the FDA's satisfaction at an acceptable cost or because there are fewer sellers of X. One cannot choose between these alternative possibilities simply by observing the lower initial demand curve.[11]

I shall make the choice by comparing changes over time in demand curves for drugs introduced before 1962 with changes in post-1962 demand curves. My procedure can be most readily understood by assuming, for simplicity, that the true demand never changes and that the rate of interest is zero. Assume, again for simplicity, that there are only two periods, one before (BL) and one after (AL) any learning from experience is completed, and that prices are unaffected by the amendments. Now we compare two somewhat simplistically labeled states of the world: I, amendments are right, and II, amendments are wrong. In State I, the pre-1962, BL-period demand curve is *ADM*, but the "true" demand

[11] If the initial demand curve had been above *ADM*, one could conclude that government produced information is more valuable than any privately produced information it displaces, but there would remain the question of whether this improvement in value exceeds the extra costs of obtaining it.

curve, which we observe in period AL, is *GHEN*. The true surplus in period BL is *BGH* − *HDE*, that in the subsequent period is *BGH*. Total surplus is 2*BGH* − *HDE*. After 1962, in this state, consumer overoptimism is dispelled by FDA testing so the true demand is revealed instantly. True surplus is *BGH* in each period, and the net benefit of the amendments is the *HDE* loss suffered in pre-1962 period BL. In State II, pre-1962 consumers learn from experience that their initial evaluation of the new drug was correct, so the true demand is *ADM*, and it is observed in period BL as well as period AL. The true pre-1962 surplus is, thus, 2*ABD*. The post-1962 consumer is, in this state, simply deprived of valuable information about new drugs, so his demand for the new drug is lower than *ADM*, say, for expositional convenience, *GHEN*. The *OF* units purchased yield net benefits of *BGH* in each period. The net cost of the amendments is then 2*AGHD* or the difference between pre-1962 net benefits (2*ABD*) and post-1962 net benefits (2*BGH*).

Finally, consider the mixed case where the true pre-1962 demand lies above *GHEN* but below *ADM*. Here, true pre-1962 benefits exceed post-1962 benefits by something less than 2*AGHD*, and there is a pre-1962 loss but smaller than *HDE*. Whether the amendments confer net benefits or costs must then be determined empirically.

To implement this approach, I shall have to estimate new-drug demand curves before and after 1962. Further, for pre-1962 new drugs, I will want to estimate the demand at the time of introduction and at a subsequent time when learning from experience should be complete. The preceding discussion implies that, whatever the state of the world, the true post-1962 demand curve will be revealed instantly. This assumption will be carried forward to the empirical work, even though we cannot realistically expect post-1962 demand curves to remain precisely stationary, or, for that matter, can we realistically expect stationary pre-1962 demand curves if the amendments are wrong. Since the demand for new drugs can wax or wane for reasons unrelated to regulation, we will, as a practical matter, have to distinguish between states of the world on the basis of differential growth of pre- and post-1962 demand curves. If pre-1962 demand grows more slowly (declines more rapidly) than post-1962 demand, this differential growth will form the basis for calculating a loss like *HDE*. There is, to be sure, an amendments-are-right bias in this procedure. More rapid post-1962 growth in demand could reflect learning by experience that FDA-sanctioned information was too restricted. Then, the initial post-1962 demand is "too low" in that it entails the sacrifice of genuine benefits. These missed benefits will be assumed nonexistent, in part for procedural simplicity, but, also to impart a conservative (pro status quo) bias to the empirical results. I believe that, given the importance of the policy implications which might be suggested

by the empirical results, such a conservative bias is not undesirable. And, wherever a choice of procedure may entail bias, I shall try to make a pro amendments-are-right choice. For example, I will rule out the possibility that the amendments produce slower growth in demand for drugs after initial marketing. If post-1962 growth is, in fact, slower, then this will be attributed to nonregulatory forces, and the initial demand curve will simply be assumed to be the true demand curve for each period.

While the subsequent empirical work can be understood in the context of the simple two-period model outlined above, I shall in fact make use of the following multiperiod model which dispenses with the simplifying assumptions of zero growth in true demand, unchanged prices, and no discount on future benefits. I write the true demand for new drugs (*GHEN* in fig. 2) as

$$p = f^*(q), \tag{5}$$

where p = price and q = quantity. The true net benefit or consumer surplus from consuming new drugs, s, in any year, t, is then

$$s_t = \int_0^{q_t} f^*(q)\, dq - (p_t q_t). \tag{6}$$

The first term on the right-hand side of (6) would correspond to *OGHEC* in figure 2, and the second to *OBDC*. The actual demand at t (e.g., *ADM*) may be written

$$p = f^t(q), \tag{7}$$

so that (6) could be rewritten

$$s_t = \int_0^{q_t} f^*(q)\, dq - [f^t(q_t) \cdot q_t]. \tag{6'}$$

The assumption that f^* is, in the absence of regulation, revealed by experience, leads to the empirical identification of f^* with f^T, where T is the time required for learning. I will assume further than f^T is attained linearly, so that,

$$\frac{\partial f^t}{\partial t} = \frac{1}{T}(f^T - f^0), \tag{8}$$

and

$$f^t = f^0 + t\frac{\delta f^t}{\delta t} = \left(1 - \frac{t}{T}\right) \cdot f^0 + \frac{t}{T} f^T. \tag{9}$$

This permits us to rewrite (6′) as

$$s_t = \int_0^{q_t} f^T(q)\, dq - \left[\left(1 - \frac{t}{T}\right) \cdot f^0(q_t)q_t + \frac{t}{T} f^T(q_t) \cdot q_t\right]. \qquad (6'')$$

Note that s can be negative, since $f^0 \geq f^T$.

New drugs yield benefits for more than a single year, so the stream of annual benefits must be discounted to yield the present value of that drug's net benefits (S), that is,

$$S_t = \int_0^{\infty} s_t e^{-rt}\, dt, \qquad (10)$$

where r is an appropriate discount rate.

This procedure will be modified in light of postamendment experience. I make the strong assumption that no learning by experience is required for f^* to be revealed when the FDA approves an NDA under the amendments. Instead,

$$F^* = F^0, \qquad (11)$$

where F denotes a postamendment demand curve. If F^T happens to be smaller than F^0, this will be attributed to other market forces. Thus, for the post-1962 period, (6″) would be simply

$$s_t = \int_0^{q_t} F^t(q)\, dq - [F^t(q_t) \cdot q_t]. \qquad (12)$$

If $F^T \neq F^0$, that fact, along with any associated price changes, will be used to compute the "normal" growth or decline (g) in s:

$$g = \frac{1}{T} \ln\left(\frac{S_T}{S_0}\right), \qquad (13)$$

so that (10) would be, simply,

$$S_t = s_0 \int_0^{\infty} e^{-(r-g)t}\, dt = \frac{s_0}{r - g}. \qquad (14)$$

Since $s_0 \geq 0$, (14) can never be negative.

If $F^T \neq F^0$ and $F^0 = F^*$, then this implies modification of the identification of f^* with f^T. The modification to be employed will be

$$f^* = \min\left[\left(\frac{f^T}{f^0}\Big/\frac{F^T}{F^0}\right) \cdot f^0, f^0\right]. \qquad (15)$$

That is, the differential growth in demand between the pre- and post-amendment period will be used to find f^*, if demand did in fact grow more slowly (fall more rapidly) prior to the amendments. The f^* of

(15) will then be substituted for f^T in (6″). Since f^* also grows by g, (10) could then be written, for the preamendment period,

$$S_t = \int_0^T s_t e^{-rt}\, dt + e^{-rT} \frac{s_T}{r - g}. \qquad (10')$$

The 1962 amendments would then confer positive net benefits if the value of S in (14) exceeded that in (10′). This could occur if, for example, there were great losses due to inefficacy, so that the first term on the right-hand side of (10′) was very small or negative. If, on the other hand, the amendments' restriction of privately produced information reduced s_0 in (14) substantially compared with, say, s_T in (10′), then S in (10′) would exceed that in (14), and there would be a net social cost to the amendments.

Drug Prices

The preceding discussion has focused on shifts in the demand curve for new drugs. However, shifts in demand may induce sellers to change prices and thus change consumer surpluses. Such demand-induced price changes would tend to increase the surplus produced by the amendments in either State I or State II. If, for example, *OB* is the seller's profit-maximizing price when the demand curve is *GHEN*, a higher demand would, under appropriate supply conditions, cause sellers to charge more than *OB*. Therefore, even if the amendments are "wrong," the consumer would, in their absence, have received a net benefit less than *ABD*, and his loss due to their error is less than *AGHD*. Similarly, in State I, the high initial demand in the absence of the amendments would engender a price above *OB*, and, therefore, the losses of learning from experience would exceed *HDE*.

The amendments have, however, also affected the cost of developing and marketing new drugs, and the effects of these costs on prices render the overall impact of the amendments on new drug prices ambiguous. The quantitative limit on seller-provided information would, standing alone, lower marketing costs. The associated price effects would complement those just discussed, again, independently of whether the extra information would have been "good" or "bad."[12] However, the important proof-of-efficacy and clinical testing provisions of the amendments work to increase new-drug development costs and prices. These provisions serve to increase direct expenditures for R & D and increase the uncertainty of their payoff. Since the testing takes time, the capital costs of the investment in new-drug development are also increased. These costs appear

[12] Where the extra information would have been worthwhile, the price of a properly defined drug-information bundle is increased by the quantitative restriction, but the price per pill falls. Consumers simply pay a little less for a much inferior product package.

to be substantial.[13] We cannot then know a priori the net effect of the amendments on new-drug prices.

There is a similar ambiguity in connection with the effects of the amendments on competition. The proof-of-efficacy requirements and the associated restrictions on drug advertising were designed in part to stimulate price rivalry. If the seller could not "artificially" differentiate his new product, the price he could get for it would be more sensitive to those of close substitutes. The other side of this, though, is that, if the product never gets to the market, a source of new competition for existing sellers is removed. Since the amendments have proved an effective barrier to entry, there is at least the possibility that they have weakened rather than promoted price competition in the drug market generally. I shall therefore investigate the effects of the amendments on prices of both old and new drugs.

Summary

The 1962 drug amendments sought to reduce the costs incurred by consumers for ineffective and unsafe drugs. To the extent that this goal has been attained, we would expect to see demand curves for new drugs which are higher and/or rising more rapidly after 1962 than before. We would also expect to see these demand changes complemented by reduced new-drug prices resulting from reduced information expendtiures by sellers or increased price rivalry among them. However, the benefits produced by the amendments should not have been costless: some of the drugs and some of the information kept from the market would, unless regulators are omniscient and dealing with them is costless, yield net benefits. These costs (forgone benefits) will be manifested in a smaller difference in the level and rate of growth of pre- and post-1962 new-drug demand curves. Similarly, certain costs imposed by the amendments on

[13] The effects on R & D cost may be estimated from a time series of real R & D (using the GNP deflator) per "NCE equivalent." An NCE equivalent is defined as 1 NCE + .30 new combination product + .16 new dosage form; the weights are Schnee's (1970, p. 77) estimates of the relative R & D cost of different new drug types. Following Schnee's estimates of development time for these types of new drugs, the number of NCE equivalents appropriate to any year's R & D is a 3-year moving average centered about 1 (new combinations and dosage forms) or 2 (NCEs) years later. Prior to 1960, real R & D per NCE equivalent was increasing at 14.8 percent per year (the correlation coefficient with time is +.96). When this rate of increase is extrapolated forward, however, post-1962 values are consistently underpredicted. For 1965–69, the extrapolated values average about half the actual values, that is, the amendments appear to have doubled the R & D costs per NCE. Even with only five observations, this average difference is over 10 times its standard error. These extra R & D costs come to between $5 and $10 million per NCE equivalent, or roughly a year's sales for a fairly successful NCE. This then implies an increase in the unit cost of a new drug at least equal to the cost of capital, and each year of delayed payoff to the R & D would inflate that increase by one plus the cost of capital. It appears that the actual delay in payoff due to the amendments is at least 2 years (Peltzman, in press).

new-drug producers and the reduced competition from new drugs facing sellers of old drugs would work to offset any reduction of drug prices. The primary object of the subsequent empirical work is to establish the order of magnitude of the resultant of these forces.

IV. Estimates of the Costs and Benefits of the 1962 Amendments

A. Consumer Evaluations in the Drug Market

This section derives demand curves for new drugs and uses them to draw inferences about changes in the consumer surplus generated by new drugs since passage of the amendments.

Data

Most of the data used in this section are taken from the *National Prescription Audit* (*NPA*), and they have been described previously,[14] but some of their shortcomings (for present purposes) deserve mention. The output measure to be used will be number of prescriptions sold and the corresponding price will be average receipts per prescription. Further, since penicillin may be a poor substitute for tranquilizers, the unit of observation is not "the" drug market. However, the relevant submarkets ("therapeutic categories") are defined technologically, by similarity of the chemical properties of the members. The potential for measurement error in these data is, of course, substantial. The more expensive prescription may be the cheaper mode of therapy; some members of one category may be closer substitutes for those in another rather than the same category, and so forth. Much of the measurement error will simply have to be accepted for the sake of empirical implementation. Prescriptions for existing members of a therapeutic category will be treated as perfect substitutes for each other, but as imperfect substitutes for prescriptions for new members. The cross-elasticity of demand and supply for drugs in different categories is assumed to be zero. However, the potential measurement error will be taken into account in interpreting the results and in designing the relevant sample.[15]

[14] See above, n. 8.

[15] To minimize the effect of errors in categorization, minor therapeutic categories (fewer than a million prescriptions in most years' samples), and minor new drugs (fewer than 1 percent of all category prescriptions or sales) are excluded from the sample. This is done because we wish to examine the behavior of the "typical" new drug within the typical category. Where a new drug gets an unusually small share of a category, it is presumed to be related in demand to only a part of the category, so, for this drug, the category is too comprehensive. If the new drug is related in demand to drugs outside its defined category, the resulting exaggeration of its importance will be most serious if the defined category is small. I also exclude categories where new drugs account for over half of prescriptions or sales in the current or any of the 3 preceding years. This kind of innovation essentially creates a new category, and the new drugs are presumed to have no good substitute or none that are really "old" drugs.

The data are sampled from a period spanning the 1962 amendments. The amendments are presumed to have affected the markets for new drugs beginning in 1964, and data on postamendment new drugs are sampled for 1964–70. Since new drug introductions declined after 1962, a similar-sized sample of preamendment new drugs is drawn from only the 3 years 1960–62, just prior to the amendments. (The innovation rate for these 3 years was about 10 percent below the pre-1962 average, so the resulting estimate of pre-1962 demand will be conservative.)

Model

Given the assumption that new-drug prescriptions within a therapeutic category are perfect substitutes,[16] the demand for new drugs may be written

$$q_{nt} = f(p_{nt}, p_{ot}, X_t), \tag{16}$$

where t denotes a particular year, q_n = number of prescriptions for new drugs in a therapeutic category per unit of time, p_n = the price per q_n, p_o = the price of imperfect substitutes for new prescriptions, X = a vector of all other factors affecting the demand for new drugs. For simplicity, p_o is identified with the average price of prescriptions for old drugs in the same category. The vector X is composed of two elements: (1) all of the systematic nonregulatory factors apart from p_n and p_o that might affect the demand for new drugs (e.g., prices of complements, income, "tastes") are assumed to be reflected in total output of prescriptions in the therapeutic category (Q_T); (2) since the 1962 amendments may have changed the demand for new drugs and since our data will span the amendments, the presence or absence of the amendments (A) is included in X. It is assumed that equation (16) is homogeneous of first degree in all nonregulatory arguments and that there are random components of q_n, so (16) may be rewritten:

$$\frac{q_{nt}}{Q_{Tt}} = f\left(\frac{P_{nt}}{P_{ot}}, A_t, u_t\right), \tag{16'}$$

where u_t is a random variable.[17] In the subsequent empirical work (16')

[16] The prescription priced above (below) average is simply more (less) than a "standard" prescription.

[17] The size-of-market deflator could have been chosen as the output of old drugs in a therapeutic category ($Q_T - q_n$). The choice of Q_T is made for subsequent computational convenience and to minimize the variance in empirical counterparts to the dependent variable arising from random output shifts between new and old drugs. Since q_n/Q_T and $q_n/(Q_T - q_n)$ are positively and monotonically related, there is no sacrifice of generality with (16'). On the basis of preliminary empirical work, I have not included in (16') a variable for growth of total category demand, though such a variable is suggested by the previous analysis of new-drug introductions. The preliminary work included past growth of category output as a demand-growth proxy. While this variable had the expected positive relationship to q_n/Q_T, the effect was insignificant and none of the results derived from the simpler formulation of (16') was materially altered.

is assumed to have the linear form:

$$\frac{q_{nt}}{Q_{Tt}} = a + b\frac{P_{nt}}{P_{ot}} + cA_t + u_t, \tag{17}$$

with a, b, and c constants; $a > 0$, $b < 0$, and the sign of c is uncertain.[18] It is being assumed here that sellers set P_n/P_o in each period and offer to sell indefinitely large amounts at that price during the period. Variation in P_n/P_o is assumed to be determined largely by nondemand-related factors, such as costs, so that any empirical estimate of (16′) will largely reflect demand relationships.[19]

Empirical Estimates

Before (17) is estimated, it is instructive to examine some of the underlying data. These indicate that the substantial decline in new drug output following the amendments has not been accompanied by a rise in the relative price of new to old drugs. Table 2 presents data on the mean relative prices and market shares of new chemical entities in the year following introduction for therapeutic categories in our sample and where NCEs were marketed. There is a perceptible decline in NCE market shares from 1960–62 to 1964–70 and a decline in the number of markets penetrated by NCEs. At the same time, the mean relative price of NCEs has, in fact, fallen, though the decrease is insignificant. It is possible that the essentially unchanged relative price of NCEs marks a departure from some trend, but this is unlikely. Table 2 contains data for 1956–57, which had levels of NCE introduction and output comparable to 1960–62; the NCE relative price then is virtually the same as that for both later periods.[20]

These data imply that the amendments have not increased the equilibrium supply price of new drugs, but they are potentially consistent with several demand effects and demand characteristics that are relevant to this study. For example, such data would be generated in a world where new drugs are essentially no more than high-priced, perfect substitutes for existing drugs, that is, where the demand curve for new drugs is

[18] The number of good substitutes for a new drug may vary across therapeutic categories, so we would, ideally, like to estimate a different b for each category. However, none of the categories have sufficiently frequent innovation to permit estimation of different relative price coefficients.

[19] Since the amendments may have affected both demand and costs, there is a potential problem in interpreting estimates of c. For example, suppose the amendments have caused P_n/P_o to rise, and q_n/Q_T has, at the same time, fallen partly because of an amendment-induced fall in demand. An empirical estimate of (17) might mistakenly attribute all of the decline in q_n/Q_T to the price increase. However, I shall argue below that this potential problem is empirically unimportant.

[20] Prices of other new drugs (combinations of NCEs and old NCEs marketed under a new trademark) also remain substantially unchanged after 1962. The 1964–69 average price relative is 1.14 versus 1.07 for 1960–62. The small difference is insignificant.

TABLE 2
AVERAGE MARKET SHARE AND RELATIVE PRICE FOR NCEs IN YEAR AFTER INTRODUCTION

NCEs Introduced in:	Annual Average Number of Therapeutic Categories with NCEs (1)	Average NCE Share of Category Output (2)	Price of NCEs/Price of Other Drugs in Category (3)
1956–57	11.0	0.132	1.223
		(0.033)	(0.063)
1960–62	10.3	0.107	1.263
		(0.019)	(0.104)
1964–69	5.4	0.064	1.165
		(0.012)	(0.050)

SOURCE.—R. A. Gosselin, Inc., *NPA*. (The 1956–57 category classification differs slightly from the later years and the coverage is less comprehensive.)

NOTE.—There are 50 therapeutic categories in the sample. Column 1 indicates the average number of these in which one or more important NCEs were introduced each year per period. Column 2 is the average number of new prescriptions accounted for by NCEs per year as a fraction of total category prescriptions for categories where NCEs were marketed. Column 3 is mean dollar value per NCE prescription divided by dollar value of other prescriptions in category. Standard errors are in parentheses.

essentially infinitely elastic since varying quantities are purchased at roughly the same price. In such a world, there would be essentially no costs (no consumer surplus lost) offsetting the benefits of the amendments. If the demand for new drugs is not infinitely elastic, then the data imply a post-1962 decline in demand. But the apparent decline might mean that the "true" demand for drugs is unchanged and merely reveals itself without a long and costly learning-by-experience process. Or the decline is "real," and reflects the reduced information content associated with new drugs under the amendments. The data do permit us to rule out the possibility that the amendments have increased the initial demand for new drugs, since that would imply a rise in post-1962 sales at the essentially unchanged price. However, an empirical estimate of (17) and of its temporal behavior is required to distinguish among the potentially valid interpretations of the data.[21]

Estimates of equation (17) are in table 3, and they rule out an infinitely elastic new-drug demand curve. The data employed are for the year following introduction for NCEs introduced in 1960–62 and 1964–69. The variable A is unity for each postamendment observation and zero otherwise. Only categories with significant NCE market penetration (1 percent or more of category prescriptions and sales) are employed in the estimates. The categories are of widely varying size, and preliminary estimates revealed heteroskedastic residuals; as might be expected, residual variance decreased with category size. To restore homoskedasticity, table 3 shows weighted regression estimates of (17), with the ratio of total

[21] The unchanged, postamendment new-drug price relative is not necessarily inconsistent with a net increase in new-drug production costs. If new-drug production is subject to diminishing returns, a fall in new-drug demand would have produced a decline in price in the absence of an increase in costs (a leftward shift of supply).

TABLE 3
ESTIMATED DEMAND CURVE FOR NEW CHEMICAL ENTITIES
(NCEs INTRODUCED 1960–62, 1964–69)

EQUATION AND DEPENDENT VARIABLE	CONSTANT	COEFFICIENTS AND SE OF:				
		P_n/P_0	Q_n/Q_T	A	R^2	SE
(E2) (q_n/Q_T) . .	0.1188	−0.0304	. . .	−0.0510	.2885	0.0687
	(0.0232)	(0.0132)		(0.0147)		
(E3) (P_n/P_0) . . .	1.6922	. . .	−2.9084	−0.3772	.8360	0.6721
	(0.1543)		(1.2588)	(0.1501)		
(E4) (q_n/Q_T) . .	0.3503	−0.1871	. . .	−0.0903	. . .	. . .
	(0.1550)	(0.0810)		(0.0519)		

SOURCE.—R. A. Gosselin, Inc., *NPA*.

NOTE.—Sample consists of 58 therapeutic categories; 31 in 1960–62 and 27 in 1964–69. Variable definitions are as follows: q_n/Q_T = number of new prescriptions for NCEs divided by total number of new prescriptions for all drugs in therapeutic category in year following introduction of NCEs; P_n/P_o = average price per prescription for NCEs divided by average price per prescription for other drugs in category in year following introduction of NCEs (average price = dollar sales divided by number of prescriptions); A = unity for 1965–70, zero otherwise; Standard errors are in parentheses; R^2 = coefficient of determination; SE = standard error of estimate (both for weighted data). Coefficients of (E4) are simple averages of those in (E2) and those implied by (E3), and their standard errors are approximate upper bounds.

category prescriptions to total prescriptions for all drugs in the year of observation as the weight. Equation (E2) reveals a significant negative relationship between market shares attained by NCEs and their relative price and a significant post-1962 decline in the level of demand. The elasticity of market share with respect to price (at sample means) implied by (E2) is only .7, which indicates that consumers treat new and old drugs as rather poor substitutes. The perceived consumer surplus from new drugs will be larger the less elastic the demand for new drugs, and so too would the perceived loss of surplus due to the postamendment decline in demand. However, in light of the measurement error in the price and quantity variables, it is risky to accept the estimates in (E2) at face value. In particular, measurement error in (P_n/P_o) will lead to downward bias in the estimated demand elasticity. However, it is possible to obtain an upper bound to this elasticity by regressing price on quantity instead of vice versa. This is done in (E3), which implies an elasticity fully 10 times that of (E2). It must be noted that the form of (E3) contains the implausible implicit assumption that sellers of new drugs predetermine output and then find a price which clears the market of this output, so (E2) is probably closer to the "truth" than (E3). However, to keep the relevant estimates of consumer surplus conservative, I will assume that the true values of the demand parameters lie exactly halfway between those in (E2) and those implied by (E3). The resulting parameter estimates are shown in (E4).

Equation (17) was also estimated for new drugs other than NCEs. The counterpart to (E2) was

$$\frac{q_n'}{Q_T} = \underset{(.0357)}{.0515} - \underset{(.0299)}{.0049}\,\frac{P_n'}{P_o} - \underset{(.0095)}{.0251}\,A, \qquad \text{(E5)}$$

where the prime refers to "other new drugs." The coefficients imply a virtually inelastic demand curve which decreased after the amendments. Taken literally, this would imply a far more substantial perceived net benefit loss due to the amendments for "other new drugs" than for NCEs. However, reversing the dependence of quantity on price generates an almost perfectly elastic demand curve which increased after the amendments. This would mean that consumers perceive no net benefits from other new drugs and that all of the value of the post-1962 increased demand is simply appropriated by price increases. That the same data give rise to these conflicting interpretations as to the shape and location of the other-new-drug demand curve, implies rather substantial measurement error. While the true demand curve is surely neither perfectly elastic nor inelastic, the risk of error in using the regression data to estimate demand parameters is much larger here than for NCEs.[22] In light of this risk, I will make what is here the most conservative assumption, namely, that the true demand is perfectly elastic. This amounts to asserting that there is no perceived net benefit to consumers from a class of new drugs with total annual sales comparable to those of NCEs. I leave open the possibility that the 1962 amendments have produced net benefits for consumers of other new drugs; demand may have grown more slowly before 1962. However, given the poor results obtained from the data on other new drugs, the most reasonable procedure might be to simply leave these drugs out of the account entirely, and evaluate the amendment and their effects on NCEs. Most of the subsequent work is therefore limited to NCE data.

The Perceived Loss of Consumer Surplus Due to the Amendments

The first ingredient in our estimate of the net benefits due to the 1962 amendments will be a gross cost: the decline in consumer surplus perceived by consumers upon their initial evaluation of information about new drugs. The higher pre-1962 evaluation of this information may, of course, reflect ignorance, so this gross cost of the amendments will have to be set off against gross benefits arising from reduced costs of learning from experience. At this stage, though, I am naïvely treating the initial demand, estimated by (E4), as the "true" demand.

The general formula for calculating consumer surplus with linear demand is

$$s = \tfrac{1}{2}(P_n^a - P_n)(q_n), \tag{18}$$

[22] The standard error of the average of the two estimated price coefficients is so large that it fails to rule out either essentially perfectly elastic or inelastic demand.

where the a superscript refers to the vertical intercept of the demand curve. In terms of the variables in (E4), equation (18) would be:

$$s = \tfrac{1}{2}\left[\left(\frac{P_n}{P_o}\right)^a - \left(\frac{P_n}{P_o}\right)\right]\left[\frac{q_n}{Q_T}\right] \cdot P_o Q_T. \qquad (18')$$

An approximation to the total of (18′) over the whole drug market can then be obtained from the parameters and the appropriate sample means of (E4) and the value of P_oQ_T for categories with NCEs.[23] To provide comparable dollar values, P_oQ_T is measured in terms of the 1970 drug market. Specifically, the aggregate of P_oQ_T for all categories with NCEs is divided by the aggregate for all sample categories in each year, and the subperiod averages of this ratio (.235 before and .231 after the amendments) are multiplied by the 1970 value of P_oQ_T for the whole drug market ($5.2 billion).[24] This permits (18′) to be evaluated as $51.9 million per year prior to the amendments and $9.9 million per year subsequently; the perceived loss in consumer surplus due to the amendments is thus $42.0 million annually for any year's flow of NCEs.[25] Now, since any year's NCEs will yield benefits over many years, the stream of these annual benefits must be converted to present values. For the moment, I will treat the stream of benefits as a perpetuity with an unchanged average annual return. The return is, however, uncertain, since the (growth of) future demand for any set of new drugs and its competitors will fluctuate. The appropriate discount rate for the stream of expected NCE benefits will therefore be the annual rate of return in activities with

[23] The appropriate sample means are the root mean square of q_n/Q_T and its associated P_n/P_o. Use of the simple average of q_n/Q_T understates aggregate surplus; surplus for below average q_n/Q_T is overvalued by less than the undervaluation of surplus for above average q_n/Q_T.

[24] This is essentially the value of prescription sales at retail outlets as estimated from *NPA* data. The *NPA* reports estimated sales at the manufacturers' level, which they estimate average 0.48 of retail value. I have excluded drug sales to hospitals, since these data are not used to estimate the relevant demand curve. Such sales are roughly one-third those of manufacturer sales to the retail market, so our surplus estimates may be considerably understated.

[25] The data underlying these estimates are as follows: variable $(P_n/P_o)^a = 1.872$ in the preamendments period and 1.390 in the postamendments period; $(P_n/P_o) = 1.199$ and 1.094, respectively; $(q_n/Q_T) = .1259$ and .0554, respectively. These data assume that only the height, and not the slope, of the demand curve has changed. When (E4) was reestimated to allow for change in slope, the resulting difference in surplus estimates increased. However, since the change in slope is insignificant, it is ignored here. To check the sensitivity of the calculations to use of weighted regressions I recomputed surplus from the unweighted analogue to E4:

$$\frac{q_n}{Q_T} = \underset{(.2213)}{.5353} - \underset{(.1385)}{.3399}\,\frac{P_n}{P_o} - \underset{(.0502)}{.0785}\,D.$$

The demand schedule implies annual surplus of $42.1 million pre-1962 and $14.8 million post-1962. The difference remains substantial, but about one-third less than the estimates from weighted regressions.

similarly risky rewards. I will use a 10 percent rate of return, which roughly corresponds to the long-run average rate of return on investment in equities. This discount rate then implies a perceived net loss to consumers of $420 million in each year that the amendments have been effective, or about 8 percent of total annual drug sales.[26]

[26] The reader should keep clear the distinction between two benefit streams affected by the amendments: (1) benefits derived from the stream of NCEs, and (2) the stream of benefits derived from any 1 year's NCEs. The reduction in (2) is $420 million, and this is repeated every year. This calculation assumes that the decline in new-drug demand leaves unchanged the price and quantity of old drugs for each q_n. However, if the reduced value of information about new drugs leads sellers to increase information provided at each old-drug price-quantity combination, part of the $420 million gross loss on new drugs will be offset. It will be shown subsequently that the amendments have had small effects on prices of old drugs, so a higher old-drug demand should show up in higher old drug output for a given output of new drugs. To see whether this has occurred, I regressed the annual growth in old-drug prescriptions ($\dot{q}_o$) from the year prior to to the year subsequent to introduction of NCEs on the annual growth of category prescriptions ($\dot{Q}_T$) in the 4 years prior to introduction of NCEs, the ratio of q_n to $Q_{T,t-2}(q_n')$, and the dummy variable A, of table 3. (Experimentation with a price-change variable for old drugs proved unsuccessful.) This regression is meant to determine whether, holding constant the expected growth in q_o ($\dot{Q}_T$ is a proxy for this) and the encroachment of new drugs (q_n'), the growth of old-drug sales has accelerated post-1962. The result of the weighted regression for the therapeutic categories of table 3 is

$$\dot{q}_o = \underset{(.0135)}{.0035} + \underset{(.0948)}{.3590}\,\dot{Q}_T - \underset{(.1007)}{.8636}\,q_n' - \underset{(.0133)}{.0104}\,A.$$

The regression implies that, after accounting for the normal effect of new drugs on old-drug sales—an 86 percent replacement of the latter by the former—there has been no acceleration of old-drug sales following the amendments. This, in turn, implies that there is no gain in consumers' surplus on old drugs to offset the loss on new drugs. Finally, the somewhat arbitrary assumptions employed in capitalizing the net benefit streams can be checked by use of observable capital values. One such value is the R & D investment in a new drug, which, as I have shown previously (see n. 17 above), has been increased by the amendments. If one assumes that the higher R & D investment in new drugs post-1962 will be fully recovered by producers (notwithstanding the failure of relative new-drug prices to rise, this assumption is tenable [Peltzman, in press]) and, generously, that neither any other cost nor the demand for new drugs has been changed by the amendments, then the initial consumer loss (L) from the decline in R & D productivity can be approximated: $L \doteq (C - C^*)[n + \frac{1}{2}(n^* - n)]$, where C = actual post-1962 R & D investment per NCE(n), and the asterisk denotes values expected in the absence of the amendments. This formulation treats producers as "selling" NCEs at a "price," collected over time, but equal in present value to the R & D investment. The post-1962 decline in n is attributed to the post-1962 rise in this price. If this implied demand for NCEs is linear, the present value of consumer loss in any year is the rise in R & D cost for that year's NCEs [$n(C - C^*)$] plus the surplus forgone on NCEs that are not produced because of the cost increase [$\frac{1}{2}(C - C^*)(n^* - n)$]. To evaluate L, the predicted post-1962 values of the R & D cost regression in n. 17 above are used as estimates of C^*. Since C is measured per "NCE equivalent," the predicted post-1962 values of (E1) are multiplied by 3.03, the pre-1962 average ratio of NCE equivalents to NCEs, to generate n^*. Further, for consistency with C and C^*, n and n^* are 3-year moving averages centered 2 years subsequent to the year in which R & D funds are spent. The 1963–69 averages of these variables are $n = 36.1$, $n^* = 129.9$, $C = \$13.4$ million, $C^* = \$6.9$ million (1970 dollars). I estimated L for each year, 1963–69, and the average estimate (1970 dollars) was $523.0 million, or about $100 million more than the loss I had estimated from new-drug demand curves.

TABLE 4
WEIGHTED AVERAGE MARKET SHARES AND RELATIVE PRICES FOR NEW DRUGS, 1 AND 4 YEARS AFTER INTRODUCTION

DRUGS AND SUBPERIOD	MARKET SHARE (q_n/Q_T)		RELATIVE PRICE (P_n/P_0)	
	1 Year after Introduction	4 Years after Introduction	1 Year after Introduction	4 Years after Introduction
NCEs introduced:				
1960–62	0.083	0.083	1.414	1.327
	(0.017)	(0.020)	(0.144)	(0.124)
1964–69	0.039	...	1.209	...
	(0.008)		(0.045)	
1964–66	0.049	0.038	1.184	1.221
	(0.012)	(0.013)	(0.061)	(0.051)
Other new drugs introduced:				
1960–62	0.064	0.077	1.133	1.130
	(0.011)	(0.014)	(0.026)	(0.023)
1964–69	0.024	...	1.206	...
	(0.005)		(0.029)	
1964–66	0.025	0.023	1.231	1.192
	(0.004)	(0.004)	(0.042)	(0.040)

SOURCE.—R. A. Gosselin, Inc., *NPA*.
NOTE.—Data are averages for those categories where new drugs were introduced, weighted by category share of total drug prescriptions. Standard errors are in parentheses.

The Reduction in Waste on Inefficacious Drugs

The amendments would be imposing an annual net burden of $420 million on drug consumers only if they never helped save consumers money on ineffective new drugs. But it is precisely such savings that the amendments are designed to produce. To estimate the magnitude of these savings we must examine the behavior of new-drug demand over time. If the amendments have been dealing effectively with what once was an important problem, we should see the difference between pre- and post-amendment new-drug demand narrowing over time, since the pre-amendment consumers would have been abandoning the ineffective drugs that the amendments now screen out. Some relevant data is presented in table 4. I am assuming that 4 years experience with a new drug is sufficient to reveal its true value. While choice of this period is somewhat arbitrary, it is in part forced by the data. A longer period would have left an unreliably small sample of post-1962 drug data.

These data reveal a remarkable stability in the demand for new drugs over time, and, what is most important here, there is no substantial difference in this respect between pre- and postamendment new drugs. None of the intertemporal differences in NCE relative price or market shares is significant for either subperiod. We shall however, have to accept the substantial risk of error in identifying the small differences that are present with changes in population means to attribute any benefits to the 1962 amendments. First I assume that any intertemporal change

in demand is one of intercept rather than slope.[27] Then, it will be seen that both pre- and post amendment NCE demand fall slightly over time. In the preamendment period, there is a fall in price with no increase in quantity, while the postamendment decrease in quantity exceeds that expected from the small rise in price.[28] However, the post-1962 NCE demand curve falls by less than its pre-1962 counterpart. The data imply that the vertical intercept of the former falls by 0.026 versus 0.087 for the latter. This .061 difference can be interpreted as the difference in intercept between the initial and true demand curve for NCEs prior to 1962, since it is assumed that all of the difference is due to the greater incidence of inefficacious drugs prior to 1962. The implied true demand curve can then be used to estimate the true consumer surplus for NCEs (*GHB* in fig. 2) and the waste due to initial ignorance of their true value (*HDE* in fig. 2). Since the difference between initial and true demand is so small, it is not surprising that the difference between perceived and true surplus is small and that the waste is trivial. The estimated true surplus for pre-1962 NCEs in the first year after introduction is, in fact, $43.0 million and the estimated waste only $0.4 million. The conclusion to which these data point is that the forgone consumer benefits of NCEs kept from the market by the amendments substantially exceed the waste avoided on inefficacious drugs.

Since ignorance is assumed here to be dispelled by experience, this conclusion can only be strengthened by extending the relevant benefit and cost estimate beyond the first year in which any set of NCEs is marketed. Such estimates were made on the assumption that both the true demand and the pre-1962 gap between initial and true demand decreased linearly for the 4 years after NCEs were introduced. Similarly, prices and quantities for intermediate years were estimated by linear interpolation of the terminal values. The resulting estimates are in table 5. The preamendment surplus, net of waste, actually increases in spite of the small decline in true demand. This increase is due to an increased dispersion of market shares wihch is not repeated for the post-1962 sample.[29] There is, consequently, a small decline over time in the surplus from post-1962 drugs.

Table 5 also provides estimates of (10′) and (14). These are derived by assuming that the pre-1962 growth in s_t ends abruptly at $t = 4$, and that the permanent subsequent growth in s is that of the post-1962 series (about -2 percent per year). If the benefits streams are perpetual, the

[27] This assumption was tested by reestimating (E4) on year-after-introduction and 4-years-after-introduction data for the relevant subset of data. The resulting difference in the coefficient of price was less than its standard error.

[28] From (E4), a (1.221–1.184) rise in price should have produced only a 0.007 fall quantity rather than the 0.011 observed fall.

[29] The increased dispersion raises the root-mean-square market share, which is the quantity at which surplus is evaluated, even though average market share is unchanged.

TABLE 5
ESTIMATED "TRUE" NET CONSUMER SURPLUS FOR 1 YEAR'S NCEs IN YEARS FOLLOWING INTRODUCTION

Years after Introduction	Preamendment NCEs ($ Millions)	Postamendment NCEs ($ Millions)
1	42.6	9.9
2	49.1	9.7
3	55.9	9.6
4	63.2	9.4
Present value of surplus stream for:		
Perpetual stream	491.0	82.4
15-year stream	397.3	67.3

NOTE.—True net consumer surplus is the estimated consumer surplus for the true demand curve less any waste for ineffective drugs. Waste is assumed zero for postamendment NCEs. See text for method of calculation.

amendments are imposing a net loss on consumers of roughly $400 million (i.e., $491.0 − $82.4 million) per year. If it is assumed that benefit streams from new drugs last for only 15 years, the estimated net loss is about $330 million annually.[30]

The reader is cautioned against a too literal interpretation of these estimates. They are best regarded as indicators of relevant orders of

[30] The reduced variability of post-1962 drug demand does confer a benefit which is left out of account in table 5 because it is difficult to measure precisely. The benefit arises because inability to perceive true demand immediately imposes a cost regardless of the error of the initial forecast. In the case of an overoptimistic forecast, the consumer buys too much initially, and, as we have seen, his loss is the area *HDE* in figure 2. There is also a similar loss if the initial forecast is too pessimistic. Suppose, for example, that the true demand is, in fact, *ADM* but that the initial demand is only *GHEN*. In this case, the consumer buys too little. With full information he would buy *OC* instead of *OF*, and he therefore sacrifices the surplus on *FC* units until he learns the true value of the drug. This sacrifice is also equal to *HDE*. Since *HDE* increases with the gap between initial and true demand, the consumer will be better off the smaller this gap regardless of its sign. Now, while we have seen that, on the average, initial demand is an essentially unbiased predictor of true demand both before and after 1962, the dispersion about the average (i.e., the average absolute error) is apparently greater before 1962. For pre-1962 NCEs, the standard deviation of the change in market share over the 4 years following introduction is 4.3 percent compared to 3.7 percent after 1962. This difference is statistically insignificant, and factors other than initial consumer ignorance affect both of these dispersions (e.g., discovery of new applications for a drug). However, we must assume that none of these other factors are operative to estimate the value of the reduced post-1962 variability. This estimate entails evaluating *HDE* with *HD* set equal to the standard deviation of market share changes in each period. I assume that the initial error of prediction is revealed and adapted gradually so that the fourth-year error is zero. The resulting estimate is that the 4-year cost of variability for a year's NCEs was $10 million prior to 1962 and $7 million subsequently, or a difference under $1 million annually. It is surprising in this context that, relative to the smaller average market share, variability of post-1962 market-share changes exceeds, though insignificantly, its pre-1962 counterpart. If consumers are made cautious toward all new drugs by the introduction of many ineffective drugs, one might conjecture that the temporal stability of pre-1962 market shares is the resultant of growing use of the effective drugs by cautious buyers and declining use of ineffective drugs. On this argument, the 1962 amendments, by removing uncertainty about product quality, would reduce the need both for caution and gradual discovery of the ineffective drugs. But this argument implies a smaller relative variability in post-1962 market share changes, which we do not observe.

magnitude. Treated this way, the estimates imply either that the magnitude of the problem of ineffective new drugs prior to 1962 was trivial or that the ability of FDA regulation to reduce the problem is small. At the same time, the reduced flow of new drugs due to the amendments is imposing net losses on consumers which are the rough equivalent of a 5–10 percent excise tax on all prescriptions sold. The general thrust of this conclusion holds up when data on new drugs other than NCEs are examined. Table 4 shows the same temporal stability in relative price and output for these drugs both pre- and post-1962 as for NCEs[31] These data imply then that any savings on inefficacious drugs due to the amendments would, as with NCEs, not compensate for forgone benefits from drugs kept from the market. Given our conservative assumption that net benefits from other new drugs are zero, these data should strengthen confidence that the estimated net loss from the amendments is not exaggerated.

The conclusion that the 1962 drug amendments have taxed rather than benefited drug consumers is sufficiently startling to require corroboration. I have thus far relied completely on the consumers' own evaluations of drugs to measure benefits and costs. I next examine evaluations of presumably more sophisticated (non-FDA) "experts." The purpose here will not be to develop an alternative "paternalistic" measure of costs and benefits. Nevertheless, the working assumption will be that "expertise" entails the ability to discover the "true" consumer interest. Thus, if there are pervasive differences between expert and consumer evaluations and if these are reduced by FDA supervention for consumers, some doubt will be cast on the magnitude of the net costs we have adduced to the amendments.

B. Expert Drug Evaluations

The effectiveness of new drugs, or their superiority over old drugs, is uncertain. Therefore, in addition to the explicit cost of the drug, the buyer bears a risk cost related to the probability that the drug will be ineffective. This cost is the product of the loss if a new drug is ineffective and the probability that a new drug will be ineffective. I test here the null hypothesis that this probability, which is a proxy for the expected cost of inefficacy per new drug unit, has declined since 1962. Given the decline in drug innovation, truth of this hypothesis is necessary, but not sufficient, for the amendments to yield net benefits. However, our estimate of the

[31] If anything, pre-1962 other-new-drug demand increases (quantity rises with price unchanged) while post-1962 demand falls (price and quantity fall) over time. However, given the relevant standard errors, the most prudent conclusion would be that demand is unchanged over time in both periods.

magnitude of reduced inefficacy costs is so small that confidence in it should be weakened by strong evidence for the null hypothesis.

I test the null hypothesis by examining its implications for the behavior of three groups who are presumably more knowledgeable about new drugs than the ordinary consumer: hospitals, expert panels employed by state public-assistance agencies, and the American Medical Association's Council on Drugs.

1. Hospital Drug Purchases

Hospitals account for about one-fourth of the value of manufacturer drug shipments. Their drug-purchase decisions will often reflect the prescribing habits of the same physicians who are prescribing for the out-of-hospital market. However, to take advantage of large-scale purchase economies, many larger hospitals limit the bulk of their inventory to a standardized drug list (formulary) developed by a specialized committee. Doctors are then encouraged or required to prescribe from the formulary (Jones and Follman 1971). There is then enough difference in the putative sophistication underlying hospital and nonhospital drug-purchase decisions to make a comparison of the two meaningful. While that difference might be larger in some cases—for example, hospitals affiliated with teaching or research programs—comprehensive data is available only for the hospital universe. These are dollar sales to hospitals of drugs classified into the same therapeutic categories employed for the out-of-hospital market.

If sophisticated hospital purchasers have always been able to discern ineffective drugs more easily than overoptimistic, unsophisticated, ordinary buyers, then we should observe: (1) prior to the amendments, new drugs took a substantially greater share of the nonhospital than the hospital market; (2) after the amendments, this difference narrows or disappears; (3) there is no change in the pre- and postamendment hospital market share of new drugs. The data in columns 1 and 2 of table 6 support all three implications strongly. The same pre-1962 new drugs took over twice their hospital market share in the nonhospital market (col. 1); that difference is substantially eliminated for post-1962 drugs (col. 2); and there is virtually no difference between pre- and post-1962 hospital market shares (row 1, cols. 1 and 2).

Before these data can support the hypothesis of an amendment-induced decline in the incidence of inefficacious drugs, one must, however, examine the implications of consumer learning by experience. If the core of efficacious drugs commands the 4–6 percent share characteristic of the hospital market in both periods (and the nonhospital market after 1962), then we would expect: (1) the nonhospital market share will gravitate toward this figure over time, as consumers learn from experience, (2) the hospital market share will remain stable over time since the initial

TABLE 6
WEIGHTED AVERAGE PERCENTAGE OF THERAPEUTIC CATEGORY SALES ACCOUNTED FOR BY NCEs, HOSPITAL AND NONHOSPITAL MARKETS, BY YEARS AFTER INTRODUCTION

	1 YEAR AFTER INTRODUCTION		4 YEARS AFTER INTRODUCTION	
MARKET	Pre-1962 (1)	Post-1962 (2)	Pre-1962 (3)	Post-1962 (4)
Hospital	5.59	4.87	11.78	6.47
	(0.85)	(1.10)	(2.06)	(3.73)
Nonhospital	14.02	4.67	13.60	4.14
	(2.11)	(0.81)	(2.56)	(1.21)
t-ratio, hospital/nonhospital	−4.67	0.31	−1.03	0.59

SOURCE.—R. A. Gosselin, Inc., *NPA*, nonhospital data; R. A. Gosselin, Inc. (1971), hospital data.
NOTE.—Sample comprises NCEs with sales to both markets (a few NCEs are sold only in one market). Percentages are weighted averages of (NCE sales/total sales in category) × 100 in each market. The weight is the ratio of category to total drug sales in each market. Standard errors are in parentheses. Row 3 is the ratio of the average difference between hospital and nonhospital sales in category (weighted by ratio of category to total drug sales in both markets) to its standard error. Columns 1 and 3 employ NCEs introduced in 1960–62, column 2 those introduced in 1964–69, and column 4 those introduced in 1964–67. The column 2 values for drugs in column 4 are 5.45, 5.06, and 0.24 for rows 1–3, respectively.

judgments by hospital buyers are accurate. The data in columns 3 and 4 of table 6, however, reveal a startingly different pattern. It is the hospitals rather than the ordinary buyers who are the "slow learners." Pre-1962 NCEs maintained their share of the nonhospital market over time, but fully doubled their share of the hospital market. The net result is that, after 4 years, hospitals were just as enthusiastic buyers of pre-1962 NCEs as ordinary buyers had been all along (the col. 3 difference in market shares is insignificant). And, with the onset of the amendments, hospitals ultimately find themselves about as restricted as ordinary buyers —fourth-year purchases of both groups are about half the pre-1962 level (cf. cols. 3 and 4).

These remarkable results are difficult to understand. Perhaps they reflect risk aversion by large institutions where one wrong decision will inevitably affect many patients and thus be widely publicized, or perhaps they reflect only the slowness of committee decision making. In any case, they surely provide no support for the hypothesis that the amendments have selectively kept inefficacious drugs from the market. Indeed, a most intriguing aspect of the table 6 data is the rather close agreement between the permanent effects of the amendments and the temporary effects of overcautious hospital purchases. In both cases, half the effective new drug sales are kept from the relevant market.

2. State Public-Assistance-Program Formularies

In recent years, there has been a substantial increase in prescription drug sales which are financed from public funds. Under various state and

local general public-assistance and medical assistance programs, pharmacies are reimbursed for prescriptions provided at no or small charge to the program clients. In an effort to control drug expenditures under these programs, several states have developed formularies listing drugs eligible for reimbursement. Reimbursement for drugs not in the formulary is allowed only in unusual circumstances and/or requires extra effort by the physician.[32] While the method by which these formularies are compiled varies considerably, some of the larger states delegate the task to specialized committees employing consultants with pharmacological expertise. Two formularies so compiled, those of California and Illinois will be used here. Their general intent is to provide a list of the cheapest effective remedies for the range of symptoms likely to be encountered by prescribers. As such, they might be expected to screen out Senator Kefauver's bête noir, the high-priced therapeutic equivalent to what is already on the market.

If many drugs introduced before the amendments and few of those introduced subsequently are ineffective, the former should have disproportionately sparse representation in the state formularies. That is, when drugs in the formularies are classified by date of introduction, the preamendment set should constitute a smaller fraction of all preamendment drugs than its postamendment counterpart. (Many drugs introduced in either period will not appear in a formulary because, for example, they treat uncommon conditions.) This hypothesis was tested by a χ^2 test for independence of classification. The question asked is, Does the likelihood of an NCE's appearance in the state formulary depend on its date of introduction? The data in table 7 reveal that, in one case (Illinois), the answer is "no"; in the other it is "yes," but it is the preamendment drugs which are more likely to appear. Some of the "poor" performance of post-1962 NCEs might be attributable to bureaucratic inertia toward the newest drugs, so I replicated the χ^2 test by using only 1964–67 NCEs. The results are basically unchanged: χ^2 for Illinois remains insignificant while that for California declines only to marginal insignificance. These data seem to imply that one set of experts (formulary committees) is no more likely to conclude that a drug is effective when it has been defined effective by other experts (FDA) than when it has not.[33] This inability of independent expert groups to improve on the consistency of a random number table might imply that inefficacy is unmanageably difficult to define or that it is empirically trivial. Neither circumstance

[32] For example, Illinois will not grant reimbursal for a nonformulary drug unless the prescriber has secured approval of a written request to the Illinois State Medical Society.

[33] Replication of these tests in the future may show more consistency among experts. The National Academy of Sciences is reviewing the efficacy of all pre-1962 drugs, and the FDA is empowered to remove inefficacious old drugs from the market. Illinois, however, alerts physicians that drugs deemed ineffective by the NAS review may be deleted from the formulary prior to any FDA action (Illinois Department of Public Aid 1971).

TABLE 7
NCEs Classified by Date of Introduction and Appearance in State Formularies of California and Illinois

Date of Introduction and State	Number of NCEs Listed in Formulary	Number of NCEs Not Listed in Formulary	Total
Illinois:			
1946–62	158 (155)	358 (361)	516
1964–70	31 (34)	82 (79)	113
Illinois total	189	440	629
California:			
1946–62	221 (208)	295 (308)	516
1964–70	33 (46)	80 (67)	113
California total	254	375	629

Source.—Paul de Haen, Inc. (1971), NCEs by date of introduction; Illinois, Department of Public Aid (1971), Illinois; California, Department of Health Care Services (1971), California.
Note.—Figures in parentheses are expected number of NCEs with independence of classification. Summary statistics are, for Illinois, $\chi^2 = 0.46$, approximate risk of error = 0.50, $df = 1$; for California, $\chi^2 = 7.56$, approximate risk of error = 0.006, $df = 1$. "Risk of error" is the risk associated with accepting the hypothesis that the number of NCEs in each cell is dependent on classification by date of introduction.

would be conducive to a major reduction in the incidence of inefficacious drugs since passage of the amendments, and the data in table 7 are inconsistent with any such reduction.

3. American Medical Association Council on Drugs, Drug Evaluations

The AMA has, since 1905, conducted evaluations of drugs for its membership. This is today the largest such program outside government. The evaluations published in *AMA Drug Evaluations* (1971; hereafter *DE*), summarize the existing pharmacological literature on each drug reviewed and make some judgment about the likely effectiveness of the drug in its various indications. I attempted to extract from *DE* some measure of the incidence of ineffective drugs by date of drug introduction. Specifically, I sought to compile, for NCEs introduced in 1960–62 and 1964–70, the longest list of drugs of questionable efficacy. Evaluations were found in *DE* for 80 of all the 111 NCEs introduced in 1960–62 and 94 of the 113 introduced in 1964–70. These are frequently guarded and qualified, but any time *DE* suggested that a drug could be ineffective, it was classified into one of two groups: I, not effective, or II, as or less effective than other drugs. There are relatively few drugs which *DE* will label "not effective" unqualifiedly, so, in addition to these, any drug where, for example, clinical data had not yet established effectiveness or were inconclusive was placed in Group I. Group I is surely too large, since for

many of its members, *DE* is willing to recommend use for certain indications.[34] However, the bias is deliberate, since we want here to establish some upper limit to the incidence of inefficacy. A drug was placed in Group II if a less expensive alternative seemed to be available for any important indication.[35] This group is also too large, since it contains drugs which are effective in some indications. I assume pessimistically that doctors prescribe these drugs mainly when a cheaper alternative is available. Table 8 summarizes the resulting classification, and contains the results of a χ^2 test for independence of the classification from time. This test shows that ineffective drugs appear more frequently before 1962. To be sure, the risk of error in accepting the hypothesis of dependence on time is moderately high. However, the data deserve further investigation because none previously encountered are so suggestive of an amendment—induced reduction in the incidence of inefficacy.

Therefore, I estimated the dollar value of the "waste" entailed by purchase of drugs in Groups I and II in the year following their introduction. All Group I drugs were assumed to have no therapeutic value, so all consumer expenditures on them are pure waste. For those Group II drugs which are as effective as cheaper alternatives, waste is the difference in per-prescription price times the number of prescriptions of the Group II drug purchased. Where a Group II drug is less effective than an alternative, I arbitrarily assumed that equal therapeutic value could have been obtained for half the cost of a prescription for the alternative, and the resulting waste per prescription is then multiplied by number of prescriptions. The resulting average annual bill for waste, adjusted to 1970 drug sales, is $17.3 million for preamendment NCEs and $3.4 million for post amendment NCEs.[36] If these payments continue perpetually, the present value at 10 percent of waste on each year's NCEs is 10 times each figure. These present values, when compared with the counterpart estimate of surplus in table 5, imply that, on an exaggerated estimate, about one-third of surplus is eroded by waste. But, what is

[34] The following description of a Group I drug will illustrate the kind of judgments made. "Results of clinical studies to date indicate that [drug] may be useful in treating [list of conditions], but data are insufficient to permit comparison of its effectiveness with that of recommended doses of other [drugs]. The usefulness of [drug] in [list of other conditions] has not been proved." A generous interpretation of this might be that the drug is clearly effective for some conditions and possibly others. I made the pessimistic assumption that doctors are prescribing the drug only for those conditions where usefulness has not been proved, or that the apparently incomplete clinical data are too optimistic.

[35] There are two subclasses of II: (1) those labeled "as effective" as some other specified drug or any other drug in the therapeutic category; (2) those "less effective" than some other drug or group of drugs. A drug labeled "as effective" in *DE* is in Group II if the average cost of a prescription in the year following its introduction exceeds that of the specified alternative; all "less effective" drugs are in Group II.

[36] Waste each year was divided by total drug sales that year and the quotient multiplied by total drug sales for 1970 to obtain these figures.

TABLE 8
NCEs Classified by AMA Evaluation and Date of Introduction

Date of Introduction	Number of NCEs Evaluated as:			Total
	Group I	Group II	Effective	
1960–62	8	8	64	80
	(4.6)	(6.9)	(68.5)	
1964–70	2	7	85	94
	(5.4)	(8.1)	(80.5)	
Total.....	10	15	149	174

Source.—American Medical Association, Council on Drugs (1971).
Note.—See text for definition of Group I and Group II and see note to table 7. Summary statistics are: $\chi^2 = 5.53$; approximate risk of error ($df = 2$) = 0.067.

relevant for our purposes, this fraction is roughly the same for pre- and postamendment NCEs. Thus, while the amendments seem to have reduced waste, they have not, in spite of the suggestiveness of the table 8 data, reduced its incidence. Therefore, they leave consumers with a net loss. Indeed, the amount of pre-1962 waste is sufficiently small for this last conclusion to have held even if post-1962 waste were eliminated.[37]

If consumers learn from experience, it may, moreover, be unreasonable to suppose that this waste continues unabated perpetually. Indeed, it is interesting to find some agreement here between pharmacological experts and the judgment of the market place. The market share of the 16 pre-amendment drugs in Groups I and II declined an average of 12.9 percent per year from the first to the fourth year after introduction, and this is twice its standard error. Only four of the 16 drugs show increased market shares. Since relative price also declined (by a statistically significant average of 2.4 percent per year), the market-share performance implies a rather substantial decline in demand for ineffective drugs. The drug consumers' ignorance thus seems something less than invincible.[38]

The last result may provide a clue to our difficulty in finding much effect of the amendments on the incidence of inefficacious drugs. Simply put, the effective new drug will be more profitable. The ineffective new

[37] Limitation of our sample to NCEs may, however, be important here. *DE* is extensively critical of combination drugs, typically on the ground that only one component affects a given symptom and that "rational" prescribing requires the physician to select the appropriate component. Any waste calculation for combination products based on *DE*'s conclusions would be extremely difficult. The difference between the cost of the appropriate NCE bought separately and as part of a combination would have to be set off against the cost of more extensive diagnosis and the added cost of separate prescribing where each part of a combination has some expected benefit.

[38] If $17.3 million of waste decreases by something like the 15 percent per year implied here, the present value of the waste issuing from 1 year's NCEs is $69 million [17.3/(.10 + .15)] rather than $173 million, and the improvement due to the Amendments is $56 million rather than $139 million.

drug, to be sure, takes an initial market share and sells at a price roughly equal to that of other new drugs.[39] The effective drugs do not, however, experience the substantial and fairly prompt loss of market share that we find for ineffective drugs. Thus, everything else the same, the likelihood that a seller can recapture his investment in a new drug will increase with its effectiveness. These penalties imposed by the marketplace on sellers of ineffective drugs prior to 1962 seem to have been enough of a deterrent to have left little room for improvement by a regulatory agency. The reduced waste on inefficacious new drugs brought about by the amendments is simply a by-product of their reduction of the flow of all new drugs. Therefore, none of the data we have examined, whether obtained from the evaluations of ordinary consumers or experts, are likely to have been very much different if, instead of detailed regulation, an arbitrary marketing quota had been placed on new drugs in 1962.

The conclusions to which this examination of expert drug evaluation seem to point are:

1. The null hypothesis of a post-1962 decline in the incidence of inefficacious drugs cannot be accepted with tolerable risk of error.

2. To the extent that data permit measurement of its size, the costs of inefficacy seem to be small. This is implied by the similarity of new-drug-market shares in sales to buyers of varying pharmacological expertise (hospital versus nonhospital). The implication is confirmed by a direct estimate of what, according to pharmacological experts, consumers are wasting on ineffective new drugs; this is consistently substantially less than half the consumers surplus generated by new drugs both before and after 1962.

3. These conclusions are similar to those implied by the previous analysis of ordinary-consumer behavior, where we found both a trivial decline in demand for new drugs as they got older and a trivial difference in the rate of decline between pre- and postamendment new drugs.

4. That analysis assumed a gradual learning process that eliminates waste on inefficacious drugs. The market behavior of a sample of new drugs deemed ineffective by experts seems to confirm the usefulness of that assumption. Their decrease in demand and the generally stable demand for new drugs renders the losses from inefficacious drugs trivial next to the surplus generated by other new drugs.

The Effect of Drug Innovation on Prescription Drug Prices

An extreme interpretation of the rationale underlying the 1962 amendments would be that most, if not all, new drugs bring no therapeutic

[39] The 16 "ineffective" pre-1962 drugs in our sample had an average initial market share of 8.7 percent and their average relative price was 1.16. For all preamendment NCEs in our sample, these figures are 7.5 percent and 1.26.

improvement over existing drugs. The bulk of the preceding data—on market shares and prices of new drugs over time, expert drug evaluations, and so forth—belies this view, but, for present purposes, I want to accept it. If the consumer "should" but doesn't treat old and new drugs as identical, his presumed gain or loss from regulation of drug innovation will turn completely on the impact of regulation on the prices he pays for drugs. That is, if he pays \$1.50 for a new drug rather than \$1.00 for a presumably equivalent old drug, he would be saved \$0.50 if the new drug were never marketed.

This view might rationalize even the most arbitrary restriction of drug innovation, since we have seen that new drugs sell at a premium over old drugs in the same therapeutic class (see tables 2 and 4). The amendments have not increased this premium, and may even have reduced it.[40] Therefore, simple arithmetic would imply that the amendments, simply by reducing drug innovation, have saved money for consumers.

Such arithmetic would, however, ignore the effects of competition between producers of new and old drugs. If the latter face a decline in demand, because new substitutes become available, they may be expected to respond by reducing prices so that the new-drug price premium becomes unattractively large for some customers. Thus, even if all of some initial price premium for new drugs is regarded as a waste, the overall effect of reduced drug innovation on consumer drug costs is ambiguous. The corresponding removal of a source of competition for established producers may preempt sufficient price rivalry to offset any savings on high-priced new drugs.

To resolve this ambiguity, I here treat old and new drugs in the same therapeutic category as perfect substitutes and focus on the average price of all drugs in the category. I then seek to measure the net impact of drug innovation on this average. (In the absence of price rivalry engendered by it, more innovation will increase this average.) I first regress a time series of the annual percentage change in average price per drug prescription ($\dot{p}_t$) in the preamendment period on the number of NCEs introduced in each of the two preceding years ($n_{t-1,t-2}$). Since major initial sales of any of the n_{t-1} are typically attained in t, the coefficient of n_{t-1} will reflect most of the inflationary impact of the new-drug price premium. If there is a lag in response of old-drug producers, the coefficient of n_{t-2} will capture the major deflationary impact of price rivalry. The regression is:

$$\dot{p}_t = 8.652 - \underset{(.006)}{.003n_{t-1}} - \underset{(.058)}{.125n_{t-2}} \qquad R^2 = .388 \qquad \text{(E6)}$$

[40] Table 4 shows a 20-percentage-point decline in the premium after 1962. This is only barely insignificant. However, the weighted average price relative for the 1956–57 NCEs in table 2 is only 1.13. Since this is less than its post-1962 counterpoint, it is risky to believe that the premium has been reduced.

for 11 observations (1952–62).[41] Since the coefficient of n_{t-1} is insignificant and that of n_{t-2} is significantly negative, the regression implies that the dominant effect of reduced drug innovation is reduced price rivalry. Specifically (E6) predicts that a permanent annual decline of 20 NCEs would accelerate the change in drug prices by 2.5 percent per year. However, while that magnitude of NCE decline has been experienced since 1962, the predicted price effect has not. Instead, there has been a deceleration from the pre-1962 average of over 1 percent per year. This might mean that the relationship in (E6) is aberrant, or that factors exogenous to that relationship have been holding drug prices down since 1962.

To distinguish among these possibilities, I next examine cross-sectional data for the 3 years preceding the amendments. Exogenous forces are assumed to affect all submarkets equally at any moment, and the dependent variable is redefined as the deviation of the price change for a category from the average price change for all categories in the same time period ($\dot{p}'$). Instead of the number of NCEs, I use q_n/Q_T, as well as the market share of "other" new drugs (q_n'/Q_T), as independent variables. The dependent variable is measured over 2 years spanning the year subsequent to drug innovations, which is the year used to measure the independent variables. In this way, the coefficients of the independent variable reflect both any immediate inflationary impact of the associated innovation and any lagged competitive reaction. The resulting regression is

$$\dot{p}' = .329 - \underset{(5.625)}{13.230}\,\frac{q_n}{Q_T} - \underset{(5.015)}{1.216}\,\frac{q_n'}{Q_T} \qquad R^2 = .036 \qquad \text{(E7)}$$

for 153 observations (51 therapeutic categories, for 1960–62 innovations). While it is weak, the negative overall effect of NCEs on drug prices persists in the cross-sectional data, and the effect remains significant (non-NCE innovation has a neutral effect on drug prices). The magnitude of the predicted effect of reduced innovation on drug prices is, however, much smaller here than in (E6). The average NCE share of category output has declined by roughly 1.5 percentage points, and in (E7) this translates into an approximate 0.1 percentage point annual acceleration of average drug prices.

The safest conclusions from these data are, I believe: (1) It is difficult to conclude that drug innovation has a net inflationary impact on drug prices, even when innovation is regarded as producing no improvement

[41] Standard errors are in parentheses. The dependent variable is derived from a series on the average retail price of drug prescriptions from *American Druggist*. When the series was deflated by the GNP deflator, the same general result was obtained, though with some loss of explanatory power. This may reflect inaccuracy of the deflator.

in drug quality.[42] (2) If innovation has any impact on prices, it is probably deflationary, though the magnitude may be small. (3) Specifically, our estimate of a 0.1 percent annual acceleration of drug prices due to the 1962 amendments translates into a permanent annual cost to drug consumers of about $50 million.[43]

V. Summary and Conclusion

The 1962 drug amendments sought to reduce consumer waste on ineffective drugs. This goal appears to have been attained, but the costs in the process seem clearly to have outweighed the benefits. It was shown that the amendments have produced a substantial decline in drug innovation since 1962. This could have produced net benefits if the impact of the decline had been highly selective against ineffective drugs and preamendment expenditures on ineffective drugs had been substantial. Neither condition is consistent with the data. In the context of this study, the decline in innovation translates into a decline in demand for, and hence in the measured consumer surplus from, new drugs. It was then shown that this decline in demand does not reflect a substantially more realistic appraisal by consumers of the genuine worth of new drugs. Pre-1962 demand did not fall substantially after consumers had time to learn the worth of new drugs from experience (nor behave much differently than post-1962 demand), as it would if pre-1962 consumers were made initially overoptimistic by exaggerated claims of effectiveness. Therefore, the cost of any initial overoptimism which is prevented by the amendments proved small next to the surplus forgone due to reduced innovation. That conclusion was corroborated by assessments of "experts" and drug buyers presumably more sophisticated than ordinary consumers. The probability that they will assess a new drug as ineffective is about the same for pre- and post-1962 drugs. An estimate of the waste saved by post-1962 consumers on ineffective new drugs which the amendments keep from the market, based on expert rather than consumer evaluations, proved to be a fraction of the consumer surplus forgone on effective new drugs which otherwise would have been marketed. This waste saving is then simply a by-product of reduced innovation, but it is small enough so that even much more selective regulation would not provide net benefits for consumers. Finally, it was shown that the new competition

[42] Such a conclusion would be difficult even using simple arithmetic. The data in table 4 imply that, for 1960–62, the average price of all drugs is 1 percent more than the average price of all old drugs, and the deceleration of average prescription price has exceeded that amount since 1962.

[43] A permanent 0.1 percent increase in drug prices this year costs consumers $5 million this year. Since the price increase is presumably permanent, there will be a perpetual stream of such costs, whose present value is $50 million at 10 percent. A similar $50 million stream of costs is engendered every year that innovation is retarded.

preempted by the amendments has led to slightly higher prices for all drugs.

The magnitudes of these costs and benefits as of 1970 are:

1. The surplus forgone due to reduced innovation is about $300–$400 million annually.

2. Reduced waste on ineffective new drugs is trivial as deduced from the behavior of ordinary consumers or more sophisticated buyers (hospitals). An ungenerous interpretation of the drug evaluations of the AMA Council on Drugs and pessimistic assumptions about prescribing practice yields an estimated annual waste reduction of $100–$150 million. But this must be reduced by more than half in light of the decline in demand experienced by ineffective drugs over time.

3. Reduced price rivalry attributable to reduced innovations costs consumers about $50 million annually.

4. The net effect of the amendments on consumers, then, is comparable to their being taxed something between 5 and 10 percent on their $5 billion annual drug purchases.[44]

This tax might be paying for benefits left out of account here. The preceding analysis is, in fact, inadequate when applied to unusually harmful or beneficial drugs (see Peltzman, in press), and both are affected by the amendments. Some of each type may be kept from the market for some time by the information requirements of the amendments. However, an analysis of the amendments' effects on the benefits and costs of these unusual innovations indicate that they compound rather than reduce the tax (Peltzman, in press). The tax might also be partly transferred to drug producers, because of its effects on competition. However, an analysis of this issue indicates that, while the amendments have not hurt drug producers, it is difficult to rationalize them as a crypto-cartelizing device (Peltzman, in press).

This leaves a paradox: the amendments seem to have harmed their intended consumer beneficiaries. Unlike other regulation which restricts output, there is no partly offsetting transfer to producers. If their net effect is then essentially a deadweight loss, one is tempted to question the amendments' political viability. However, there appears to be no imminent reduction in the political demand for either the amendments or for similarly structured consumer legislation. Clearly, the sources of this political demand require examination.

[44] One should mention the direct budgetary cost of implementing the amendments. This appears to be relatively trivial. From 1947 to 1962, the FDA budget, deflated by the price index for general government output, rose 6.6 percent per year. In the 2 subsequent years, this accelerated to 18.0 percent. The 1964–70 growth rate was 4.4 percent. If we assume that the pre-1962 growth rate would have been maintained if the amendments had not been enacted, the 1970 budget would have been about $59 million, or $7 million lower than the actual 1970 budget. Alternatively, if we compound the 1962 budget at the slower post-1964 growth rate, the estimated 1970 budget is $15 million below the actual.

References

American Druggist. Various issues.

American Medical Association, Council on Drugs. *AMA Drug Evaluations*. Chicago: American Medical Assoc., Council Drugs, 1971.

California, Department of Health Care Services. *Medi-Cal Formulary*. Sacramento, Calif.: California, Dept. Health Care Services, 1971.

Harris, Richard. *The Real Voice*. New York: Macmillan, 1964.

Illinois, Department of Public Aid. *Drug Manual for Physicians*. Springfield: Illinois, Dept. Public Aid, 1971.

Jones, D. D., and Follman, J. F., Jr. *Health Insurance and Prescription Drugs*. New York: Health Insurance Assoc. America, 1971.

Paul de Haen, Inc. *de Haen Nonproprietary Name Index*. Vol. 8. New York: Paul de Haen, 1971.

Peltzman, S. "The Benefits and Costs of New Drug Regulation." In *Proceedings of the Conference on Regulation of New Pharmaceuticals*. Chicago: Univ. Chicago Press, in press.

R. A. Gosselin, Inc. *National Hospital Audit*. Dedham, Mass.: Gosselin, 1971.

———. *National Prescription Audit: Therapeutic Category Report*. Various issues.

Schnee, J. E. "Research and Technological Change: The Ethical Pharmaceutical Industry." Ph.D. dissertation, Univ. Pennsylvania, 1970.

U.S., Bureau of Labor Statistics. *Employment and Earnings*. Washington: Government Printing Office, various issues. (*a*).

———. *National Survey of Professional, Administrative, Technical and Clerical Pay*. Washington: Government Printing Office, various issues. (*b*).

U.S., Bureau of the Census. *Census of Population*. Washington: Government Printing Office, various issues.

U.S., Office of Business Economics. *National Income and Product Accounts of the United States, 1929–1965*. Washington: Government Printing Office, 1966. (*a*).

———. *Survey of Current Business*. Various issues. (*b*).

U.S., Congress, Senate, Judiciary Committee. *Administered Prices: Drugs*. 87th Congr., 1st sess., June 27, 1961.

Wardell, William. "The Drug Lag: An International Comparison." Mimeographed. Rochester, N.Y.: Univ. Rochester, 1972.