with the "over-all view of the book." The book was prepared in close consultation with the individuals listed as contributors to the book. During the course of these consultations they were free to voice their dissent with the "over-all view." Not a single one did; not a single one has done so since.

5) The same article contains the following statement: "This report, perhaps unavoidably, has given the entire movement associated in one way or another with the Forward Strategy a more monolithic character than it actually has."

I know of no movement—"monolithic" or otherwise—associated with the "Forward Strategy." I herewith state categorically that the Foreign Policy Research Institute is not associated with any "movement." A political movement —and the author of the article can have no other movement in mind—must be organized in order to justify the term. This institute has no connection with any political movement aimed at promoting any particular set of political doctrines or strategic concepts. Members of this institute, like most Americans, are members of one of our two great political parties and of a variety of civic, professional, and scientific organizations. The Foreign Policy Research Institute has no affinities except those that are explicit in its status as a research group within the University of Pennsylvania.

6) The author of the two articles seeks to establish a covert relationship between *A Forward Strategy for America* and another book published previously by the Foreign Policy Research Institute—namely, *American Strategy for the Nuclear Age*. According to H.M., the purpose of the latter book was to soften and prepare the way for *A Forward Strategy for America*, which, according to him, maintains that the U.S. must prepare for launching a surprise attack against the Soviet Union. Although this assertion is made repeatedly, H.M. is careful to protect himself by an ingenious literary device against the charge of having disregarded the actual text of both books. He concedes that the book does not contain a proposal for a policy of striking "a surprise knock-out blow" at the Soviets. Yet he has mastered this problem by writing as follows:

> This policy is not specifically stated in the book; it is merely the only realistic policy that follows from the premises of the book, and the members of the Foreign Policy Research Institute consider themselves, above all else, as realists.

His conclusion thus boils down to an attempt to read our minds rather than our writings. This procedure can be characterized in various ways; it cannot be mistaken for scientific method.

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I could argue with a number of the points in Strausz-Hupé's letter, but overall there is no doubt that the articles contain substantial flaws. I think the letter of censure is well deserved.—H.M.

Drugs and the Kefauver Bill

The following statement appeared recently in "Science and the news" [*Science* **134**, 89 (14 July 1961)]: "Kefauver has produced evidence that a sizable proportion of the new drugs patented and put on the market are not in any significant way new. They involve merely minor changes in the molecular structure of an already avail-

able, and perhaps unpatented, drug; their only advantage is that they can be patented, promoted as a new drug, and thus be relieved of direct competition with similar drugs identical in their medical effects. The Kefauver bill would require that a drug be significantly different in its effects as well as in the details of its molecular structure in order to be patentable."

I wish to call attention to the fact that Senator Kefauver's generalization does not apply to most psychoactive drugs, for the brain is more sensitive than any other organ to the chemical structure of a drug. Let me say in the first place that in most instances the first member of useful groups of drugs was found by accident, as a trained worker took advantage of a chance observation. Further development, however, came from the application of the principle of molecule manipulation. This applies to meprobamate (trade names, Miltown and Equanil), one of the drugs most widely used in the management of the neuroses, and chlorpromazine (Thorazine), a member of the phenothiazine group of drugs, which is employed more than any other in the treatment of the psychoses.

Mephenesin was synthesized to provide a drug affording muscular relaxation. In the course of clinical study it was noted that the muscular relaxation was sometimes accompanied by tranquilization. This finding led to the synthesis of meprobamate, which has stronger central effects than its parent substance, and today this drug is widely used as a mild tranquilizer, especially for the treatment of the neuroses, as it relieves anxiety and tension. Further development of meprobamate—namely, the formation of mebutamate—yielded a drug with less marked tranquilizing action but with intensified power to lower blood pressure. Additional molecule manipulation yielded carisoprodel, which evokes more pronounced muscular relaxation than mephobamate.

Largactil, known as chlorpromazine in the United States, was administered to disturbed psychotic patients in France because of its sedative action. This new drug, however, showed a capacity to reduce psychotic excitement not found in earlier drugs, and it has achieved wide usefulness as a strong tranquilizer. The sedatives previously employed could not relieve hyperactivity and calm the patient, nor could they reduce the intensity of hallucinations and delusions without inducing sleep. The other

phenothiazine drugs now used were developed by molecular manipulation, and they perform the same actions but to different degrees. The stronger ones require a smaller dosage and evoke lower degrees of sedation and fall in blood pressure. Convulsions and rashes are less frequent, while jaundice and a decrease in white blood cells occur more rarely than with the weaker phenothiazine derivatives. But for the advantages of the more potent members of the phenothiazine group, and their greater stimulating powers, we must pay the price of an increase in undesirable neurological effects such as tremor, motor restlessness, spastic muscular contractions, and involuntary muscular movements. The wide variations among the various phenothiazine drugs permit the discerning psychiatrist to select the one most suitable for an individual patient, through his knowledge of the greater tranquilizing action of the weaker phenothiazines, the greater stimulating effect of the stronger phenothiazines, and the characteristic intensities of the side reactions, which differ with each member of the phenothiazine group.

Altering the molecular structure of some parts of the phenothiazine molecule yields drugs which produce behavioral effects not evoked by phenothiazines. The substitution of a diethylene linkage ($-CH_2-CH_2-$) for the sulfur atom (S) produces imipramine (Tofranil), and instead of a tranquilizer we have an antidepressant drug.

These facts, and many more like them, reveal the importance of molecule manipulation in research but do not answer specifically Senator Kefauver's objection to patenting drugs which seem to have similar actions despite molecule manipulation. The diversity of reactions to the same drug by different patients is well known. It is true that most patients react in similar ways to a given phenothiazine, but it is a remarkable fact that psychotic patients who are not improved by one of two apparently equivalent phenothiazines may receive benefit from the other. Clinical use of new phenothiazine reveals that some patients who were not helped by the previously known phenothiazines respond to the new one. It would seem that, with enough patience, a phenothiazine derivative could be found to improve every schizophrenic to some degree. Such a prospect could not be realized if drugs that produce similar effects in most patients were not

developed and administered to patients whose reactions differ from those of the majority. If the restrictions suggested by Senator Kefauver were adopted, they would hinder the development of many useful drugs. This would change our present situation, so full of promise, to one of restricted output, not conducive to future progress.

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Being a research chemist in a drug firm I am perhaps biased, but I feel that a protest should be registered against Howard Margolis's account of the hearings on the Kefauver omnibus bill for regulation of the pharmaceutical industry. Margolis does not report on Senator Kefauver; he propagandizes for him.

The tenor of the article is indicated by the last two sentences: "For all these reasons a far more intense controversy surrounds the bill than a casual reading of Kefauver's bill would suggest. For the bill, on a casual reading, appears to contain nothing more than a series of minor technical changes in laws of whose existence the public is scarcely even aware." Now the changes proposed by the bill are not minor, and what is so troubling about the account in *Science* and the attitude of Kefauver is the complete failure to understand that these changes are a grave threat to the future of research in medicinal chemistry. One may just as well expect the modern theater to flourish without copyright protection.

The pharmaceutical industry has been accused of excessive price-charging by Kefauver. The industry has replied that prices are generally not excessive, and that one factor which the senator has failed to take into account with regard to new drugs is the high cost of research. Kefauver answers in his omnibus bill with licensing regulations which will effectively eliminate research. Drug prices will drop if research is stopped, but there is a catch —there will be no new drugs.

Senator Kefauver will not pay for progress. He has the viewpoint of Ortega y Gasset's "hyperdemocrat," who "wants his motor-car, and enjoys it, but believes that it is the spontaneous fruit of an Edenic tree. In the depths of his soul he is unaware of the artificial, almost incredible, character of civilization, and does not extend his enthusiasm for the instruments to the principles which make them possible" (*Revolt of the Masses*, chap. 9).

Margolis repeats, with apparent approval Kefauver's contemptible suggestion that the American Medical Association has come to the defense of the drug industry solely to protect the advertising revenues of its journals.

One expects a better understanding of science in *Science*.

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The point of the article was exactly the one made in Rogers' letter: namely, that, as the two sentences he has quoted suggest, the bill is designed to have a profound effect on the drug industry even though a casual reading might suggest merely a series of minor technical changes. The article did not say, and so far as I can see did not suggest, that the sole reason the AMA supported the industry was to protect its advertising revenues.—H.M.