

Other molecular modifications followed: perphenazine ("Trilafon"), trifluoperazine ("Stelazine"), and trimipazine ("Temaril").⁸⁵ In the mild tranquilizers field, a Dr. Berger had discovered mephenesin, a muscular relaxant, in England, and came to the United States to patent a molecular modification, meprobamate, as a tranquilizer, which was marketed by Carter ("Miltown") and Wyeth ("Equanil") in 1955. Both products were highly advertised, a condition of Wyeth's license from Carter being that Wyeth would spend at least 20 percent of total meprobamate sales revenue in promoting its sale.⁸⁶ Smith, Kline and French found itself with the potent tranquilizers and no mild tranquilizer; it then began to advertise "Compazine" as a mild tranquilizer. "Compazine" is actually much more potent than "Thorazine."⁸⁷ Medical opinion inclines to the view that none of the later modifications of the original phenothiazines has been a marked improvement. Dr. Lehmann testified: "There hasn't been a very much better one than the very first ones that came out, in the six or seven years of frantic research since then."⁸⁸ No diminution in the incidence of side effects could be demonstrated.⁸⁹

The situation in the antibiotics market is largely the same, but of greater complexity. The discovery of penicillin in England in 1929, and the further discovery of streptomycin at Rutgers University in 1943, demonstrated the possibility that many naturally occurring molds might have antibiotic properties. Many drug makers set themselves the task of the trial and error screening of thousands of soil samples. The first success was encountered at Yale University in 1947 under a Parke, Davis grant, the antibiotic chloramphenicol ("Chloromycetin") being isolated. Lederle next discovered chlortetracycline in 1948, and named it "Aureomycin." Pfizer then found oxytetracycline in 1949, and designated it "Terramycin." Pfizer managed to elucidate the chemical structure of oxytetracycline, and with the molecular structure known, molecular manipulation became possible in antibiotics, although to a more limited extent than is possible with drugs which can be made synthetically. In 1955, Pfizer developed tetracycline as a molecular modification of chlortetracycline.⁹⁰ The screening of soil samples continued. Lilly in 1952 discovered erythromycin. Pfizer in 1953 brought out a closely related analog, carbomycin, which affected the same bacteria as erythromycin, but which proved less effective in human disease than in the test tube, and which was finally withdrawn from the market in 1960.⁹¹ In 1956, Pfizer introduced another closely related analog of erythromycin, oleandomycin; and in 1957, a modification of oleandomycin, triacetyloleandomycin, which was advertised as a great advance, since the same oral dose as in oleandomycin produced somewhat higher concentrations of the drug in the blood. To offset this, Lilly in 1958 modified its original erythromycin to market it in the form of its propionyl salt, which is said to produce a higher concentration of this drug in the blood than triacetyloleandomycin.⁹² Hence, five drugs were produced to serve the purpose of one (since slightly higher doses of erythromycin could serve the same purpose as the newer derivatives). Another broad spectrum antibiotic was brought out by Lederle in 1959, demethylchlortetracycline, or "Declomycin," a slight modification of Lederle's chlortetracycline. Fewer side effects than other broad spectrum antibiotics were claimed. Not all physicians agree.⁹³ The later penicillins are patentable variations of the earlier original penicillin which the British discoverer did not bother to patent. In 1952, four American firms made a substitution of benzathine for procaine in the penicillin compound; the parties

⁸⁵ Subcomm. Report 121.

⁸⁶ Testimony of Irene Till, Hearings on Administered Prices, pt. 16, at 9208.

⁸⁷ Testimony of Dr. Heinz Lehmann of Verdun Protestant Hospital, Montreal, *id.*, pt. 16, at 9068-73.

⁸⁸ *Id.*, pt. 16, at 9029.

⁸⁹ Physicians employed by drug firms who testified sometimes found it easier to ignore side effects than one suspects their drug users could. Dr. Gibson of Merck went so far as to introduce his aesthetic preference for facial contours as the determinative criterion for evaluating the side effect of "moon face" encountered in steroid therapy. In commenting upon this side effect (caused by redundant retention of cellular fluids, a circumstance conducive to additional strain on the cardiovascular system), Dr. Gibson testified: "When those people [malnourished patients] got a moonface I think it is a desirable effect." *Id.*, pt. 14, at 8188.

⁹⁰ Subcomm. Report 116-17, 124.

⁹¹ Testimony of Dr. H. F. Dowling of the University of Illinois, Hearings on Administered Prices, pt. 24, at 14167.

⁹² *Id.*, pt. 24, at 14167-68.

⁹³ Several of the physicians who testified during the Hearings professed to see little difference among the broad spectrum of antibiotics. See *id.*, pt. 18.