may constitute questionable and/or necessary flourishes in the interest of increasing a drug's absorption rate, guarding against side effects, etc.[14]

Product development.—The category of product development includes many activities, such as experimental and clinical testing, determination of appropriate dosages and dosage forms, obtaining FDA approval for marketing new drugs, constructing pilot plant facilities, etc. Subsequent to initial marketing there would be product application work relating to long-run evaluation of the total effects of a drug, improvements in dosages, revisions of brochures, and related activities.

In an efficiently competitive drug industry, profit prospects from marketing new drugs would be moderate, and the temptation for extreme haste in product development would be correspondingly slight. It is very important that this temptation be minor, since proper testing and evaluation of new drugs is an important and time-consuming task. And, as Dr. C. D. Leake of Ohio State Univeriity has observed, "There is no shortcut from chemical laboratory to clinic, except one that passes too close to the Morgue."[15] But before certain needed reforms were legislated in 1962, many firms yielded to the temptation to rush new drugs thru the development phase and on to the market as soon as possible, limiting experimental and clinical work to the minimum acceptable levels under the old legislation, harassing FDA staff members into approving inadequate applications,[16] and even skipping such seemingly essential product development stages as pilot plant operation.[17] Furthermore, with an inflated number of drugs being clinically investigated in the expectation of reasonably rapid FDA approval, the available time of the most highly qualified investigators was soon completely employed, and recourse to less trained, less capable, and in some instances less scrupulous individuals was necessary. But drug evaluation by unqualified investigators can be worse than useless.[18]

Since the passage of the 1962 legislation, there has been much improvement in this area. More stringent requirements for approval of new drug applications have been imposed; the number of new drugs being evaluated has apparently declined, making possible an increase in the average quality of evaluations, and the morale and effectiveness of the FDA has greatly improved. This is apparently one area in which drug safety reforms may have been successful in eliminating certain economic wastes as well as improving drug quality. But it should be noted that any reduction in total drug development outlays would be likely to result from a reduction in the number of new drugs under investigation; the average cost of investigation per drug is likely to increase, and this increase is certainly in the best interest of public health.

Manufacturing of the active ingredient.—In an efficiently competitive drug industry, each stage in the production process would be carried out at minimum

---

[14] Dr. Harry F. Dowling of the University of Illinois Medical School cited an excellent example involving both molecular manipulation and the use of inconsequential additives. Lilly discovered erythromycin in 1952, and in 1953 Pfizer retaliated with a molecular shadow, carbomycin, which proved less effective in human disease than in the test tube, and was finally withdrawn from the market in 1960. Pfizer tried again in 1956 with another chemical echo of the erythromycin, eleandomycin, and in 1957 modified its own modification, called it triacetyloleandomycin, and advertised it widely as a major breakthrough in that the same oral dose as eleandomycin produced somewhat higher concentrations of the drug in the bloodstream. Lilly responded in 1958 by modifying its original erythromycin and marketing it in the form of its propronyl salt, claiming a higher blood concentration rate than could be achieved with triacetyloleandomycin. None of the four later drugs had any real advantage over the original discovery, since slightly higher doses of the original drug would have been as effective as the later variants. *Ibid.*, part 24, pp. 14167–14168.

[15] *Ibid.*, part 18, p. 10418.

[16] See testimony of Dr. Barbara Moulton, *Ibid.*, part 22, pp. 12025–12032.

[17] Lederle bypassed the Pilot-Plant Stage with its Triamcinolone. See *Fortune,* May 1960, p. 276.

[18] Dr. Maxwell Finland, Harvard University Medical School, cited an instance where a clinical investigator had reported successful treatment of 100 cases of staphylococcal pneumonia without a mortality. Since the usual mortality rate among the patients concerned is 50 percent, the drug would appear to be miraculous. But upon investigation, Dr. Finland concluded that not a single case of staphylococcal pneumonia had been present, and inferred that the investigator was incompetent to diagnose the presence of the true disease from the laboratory cultures. He concluded pointedly: "This is the sort of thing that I say is dangerous because another doctor who knows how to make a diagnosis of staphylococcal pneumonia will use that drug to the peril of his patient." Hearings on Administered Prices, op. cit., part 24, pp. 450–451.