viewers at the Cancer Institute shockingly inadequate even to establish whether the drug was fit to be tested on human patients. Within a few months the manuscript submitted to the *Journal* had been rejected, and further consideration of proposals for a test tabled until more data could be supplied. The old question of whether Krebiozen was being justly treated by the scientific community was back again in full force. What was the cause of the trouble?

If there is reason to doubt that Ivy's data was scientifically inviolable, there is also reason to doubt that it was reviewed by NCI with a very sympathetic eye. Although the Institute's letters to Ivy and Durovic (7 and 8 March 1962) stressed, among other things, the inadequacy of prior toxicity and other studies on animals, the unreliability of the bioassay used (tests on breast cancers), and the uncertainty about Krebiozen's chemical nature, or its reproducibility, high NCI officials, in private conversation, have cast some doubt on the validity of their own objections, and on whether more is being demanded of Krebiozen than of some of the other hundreds of thousands of anticancer substances that the Institute regularly screens and, in many cases, tests on human patients. The human bioassay, for instance, while not regarded as satisfactory, is far from unique in the history of drug experimentation; Krebiozen has generally been conceded to be nontoxic (although this has not been independently established); Krebiozen would not be the first drug (nor the first tested at NCI) to be active on human cancers but not on animal cancers; and finally, an NCI official closely involved with the case stated that enough information had been revealed about the method of extracting and manufacturing Krebiozen for the Institute to produce (and presumably analyze) the substance itself. This would in no way resolve the controversy, since it could always be claimed that the batch produced was not identical to the batches with which Ivy and Durovic claim to have achieved their results; but it is an interesting comment on the validity of the NCI argument that Krebiozen is still too mysterious a substance to justify its use in human patients.

On the other side, however, and despite the fact that Ivy's data were not intended to establish the efficacy of Krebiozen but only to serve as a basis for tests that would do precisely that, it must be said that Ivy's scientific house was not in very good order, and his data did not make the Institute's task any easier. Taken separately, none of the elements of Ivy's report was unprecedented; but the separate unorthodoxies when added up appeared monumental, and left the Institute with the dizzy feeling that Krebiozen could simply not be pinned down in any reliable way. Some sense of the NCI's frustration in dealing with one of its former advisers, a man who officials felt should clearly "know better." can be gleamed from the letter to Ivy from H. B. Andervont, scientific editor of the Cancer Institute's *Journal*, rejecting his manscript (1 December 1961). After three pages detailing his reasons for regarding the manuscript as inadequate, Andervont closed with a paragraph that is a cross between a plea for scientific orthodoxy: "The manuscript differs from most scientific presentations in several respects. It does not contain an introduction in which the author refers to previous investigators who were interested in stimulating RES [the method of obtaining Krebiozen from horses] to ascertain whether it is involved in the growth of tumors. It does not contain a section of materials and methods for defining clearly the preparation of Krebiozen, the response of patients, the technique for collection and analysis of data procured from physicians, and the criteria used for their evaluation. It does not contain a discussion of results in relation to other kinds of cancer treatment. A conclusion is found on page 80 of a paper consisting of 120 pages."

The misunderstandings—partly petty disagreements over form, partly deep disagreements over substance—all sprang from the initial confusion over whether an NCI test had been absolutely, or only conditionally, promised. The refusal to conduct a test on the basis of the data supplied appeared to Ivy and Durovic as treachery; to the Cancer Institute, the pressure to test on human patients a substance about which it still felt so uncertain threatened its scientific and moral integrity. Both sides, however, though they suspected each other of the worst possible motives, were unwilling to give up the idea of a test altogether, and for different reasons both began to seek the aid of other government agencies in obtaining some of the data in dispute.

As far as NCI officials were concerned, the inadequacy of the material submitted suggested that Krebiozen's sponsors simply did not have the evidence to support their claims, and they began to press the Food and Drug Administration to determine whether Krebiozen was being "investigated" in a clinical sense, at all or merely distributed for commercial purposes. At the same time, in his reply to the Institute's rejection of his data in July, 1962 (strategically withheld until NIH appropriation time again, when it appeared simultaneously as a letter to Endicott and as an entry, by Senator Douglas, in the *Congressional Record*) Ivy explained that some of the material NCI wanted—mainly extensive case histories of patients on Krebiozen—had been impossible to obtain.

Ivy attributed his own inability to collect the records mainly to the inhibitions of physicians in admitting that they had administered a drug that had been frowned on by organized medicine, and in part simply to the financial burdens the task had posed. Although he did not agree that the data was crucial to the proposed NCI test, he did suggest that lack of such data had "impeded our study of the past 12 years," and he, too, suggested that the government use its power to get the records from hospitals and private physicians.

With requests from both sides on its hands, the Food and Drug Administration could hardly avoid initiating an investigation. After a few more minor skirmishes, an investigation into both the commercial and clinical history of Krebiozen was begun in March 1963. Things were at this stage when the unresolved controversy collided with new drug laws to produce the Krebiozen panic of early June.

—ELINOR LANGER

Announcements

A department of **pharmacology** will be activated 1 July at Wake Forest College's Bowman Gray school of medicine. It was formerly part of the department of physiology and pharmacology. J. Maxwell Little, formerly head of the pharmacology section in the combined department, is chairman of the new facility.