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NEWS AND COMMENT

Cancer Institute: Expert Charges Neglect of Carcinogenesis Studies

A prominent scientist has resigned from directorship of a key program in the National Cancer Institute for reasons which, if well founded, could provoke a serious perturbation in the agency's affairs. The scientist, Umberto Saffiotti, heads the NCI's program in chemical carcinogenesis, a subject whose importance has been increasingly acknowledged by cancer epidemiologists, by regulatory agencies, and in Congress. A threatened fragmentation of the program which could prolong the public's exposure to carcinogens is one of the reasons behind his decision to quit.

NCI director Frank Rauscher pays tribute to Saffiotti's scientific expertise but regards the issue of his resignation as the result of a difference in approach to the management of certain programs under his control, which Rauscher believes could have been pushed ahead faster.

Saffiotti believes that the carcinogenesis program has long been denied the manpower necessary to keep pace with its growing responsibilities. It has only 20 percent more staff than in 1968, but almost 8 times the amount of money to administer. This year the program received only 3 of the 79 new staff positions assigned to the NCI, although Rauscher told the House Appropriations Committee that he was giving Saffiotti the highest priority possible. With a current budget of $47 million, the program conducts basic research on chemical carcinogenesis as well as developing bioassay tests for carcinogens.

Saffiotti also feels that he and other colleagues with relevant expertise have been excluded from a series of decisions on chemical carcinogenesis, the most recent being the announcement of a National Clearinghouse on Environmental Carcinogenesis, on which he says he was not consulted until a late stage. The final straw for Saffiotti was a recent decision to split away from his program the responsibility for developing bioassay tests for chemical carcinogens. The move will, in his view, compromise the scientific credibility of the tests, delay their being put into action, and increase the time that people will be exposed to the chemicals the tests may show to be carcinogenic.

Although he has been asked to remain as director for the research part of the carcinogenesis program, Saffiotti has chosen to resign altogether from the program management, lest he seem by staying to concur with the decision on the bioassay tests. He plans to take up full time research in his laboratory at the NCI. "I am glad to call it quits rather than endorse a mode of operation I disagree with," he told *Science* in an interview last week before announcing his resignation.

Saffiotti adds that a fundamental reason for resigning is his belief that active scientists have very little voice in setting policy or priorities in his division of the NCI, and that the division is being run by managers with the help of scientists rather than the other way around. Because of the growth of successive layers of bureaucracy, whose actions are not accountable to detailed peer review by scientists, Saffiotti says, "There seems to be a growing gap between the top policy-making decisions of the institute and the

expertise which is needed to make these complicated value judgments."

Saffiotti's resignation is likely to be taken seriously because he is well known outside the NCI. He has been an active researcher in chemical carcinogenesis for 20 years and has headed the NCI program since 1968. Evaluations of data by his program staff have played an important part in regulatory decisions banning various chemicals, such as the pesticides aldrin and dieldrin. As the NCI's leading expert on chemical carcinogenesis, he has given frequent testimony before congressional committees and is a key figure in the field.

NCI director Rauscher calls Saffiotti a "superb scientist" but ascribes the reasons for his resignation to a difference in managerial approach. In a brief conversation before going out of town, Rauscher told *Science* he had been unable to assign as many staff positions as he would have liked to the carcinogenesis program but that Saffiotti could have reassigned his own staff to the bioassay area. The NCI position has been discussed in greater detail by deputy director Guy Newell and by James Peters, director of the division of cancer cause and prevention, to which the carcinogenesis program belongs.

Part of Saffiotti's unhappiness about the role of scientists in NCI policy-making relates to the fact that Peters, as division director, has to make decisions affecting chemical carcinogenesis research even though he has no scientific research experience. Peters, a veterinarian by background, notes that he has a master of public health degree in epidemiology and worked for 5 years as Saffiotti's deputy in the carcinogenesis program. Asked if he has the expertise to make decisions about carcinogenesis research, Peters says that he feels perfectly qualified to do so: "While I don't have the bench-side experience that Saffiotti has, I am in a better position to make decisions because from my position as division director I have an overall view of the program's needs within the division and of its relationship to other agencies."

The specific issues which prompted Saffiotti to resign are hard to assess because he and the NCI top management are to some extent talking past each other. Saffiotti discusses the issues in terms of their impact on research, Rauscher and Peters in terms of managerial and public relations aspects. A principal point of disagreement concerns the management of bioassay tests for carcinogens, both in vivo tests in which a chemical is fed to animals for an extended period, and in vitro tests in which cell cultures are the test medium. The in vitro tests, still in the process of development, promise to be very much quicker and cheaper than the $100,000-per-chemical tests in animals.

Umberto Saffiotti

What triggered Saffiotti's resignation was a decision to split the validation of the in vitro tests from the basic research, leaving the research in Saffiotti's program and moving the validation to Peters's office. The project will not receive any more staff in Peters's office, but, according to Rauscher, it will be "in an organizational position of higher visibility and emphasis." Rauscher says he has promised Congress that the NCI would press ahead with the in vitro bioassays. "Umberto feels this has been done, I feel that more could be done. Some of the advice I have been getting from some people is that he has not been moving fast enough," Rauscher says.

Saffiotti's position is that he has been moving ahead as fast as he could, but that the tests are at an extremely delicate stage where the state of the art varies from one laboratory to another and expertise at the bench counts for almost everything. To divorce research from development at this stage will, in his opinion, crucially delay the validation of the tests. "All the experts in the field are saying, 'Go full steam ahead in developing the tests, but don't stop to test chemicals because you will get a lot of test data you can't interpret properly,' " Saffiotti observes.

Peters and Newell say that there is no question at all about Saffiotti's managerial ability, but that they believed the tests could be developed more quickly. Asked the basis for disagreeing with Saffiotti's scientific judgment, Peters says he regards the decision as managerial, not scientific, but that outside scientists were consulted. The discussions took place on an informal basis over a long period of time until the decision just emerged, Peters says. A member of the NCI advisory board says that the decision to split off validation of the in vitro tests "ought to be made with a good deal of advice from scientific people who are not members of the NCI. That is what advisory committees are for."

Rauscher, Newell, and Peters also seem to hold Saffiotti to blame, though without directly saying so, for the bottleneck that has arisen in assessing and disseminating the results of in vivo tests. Some 200 chemicals have been put through animal feeding tests, but the results have not yet been published. Saffiotti says that he warned of the bottleneck 3 years ago, at the time the tests were started, but never received the staff he needed to get the results out. He was unable to transfer staff from elsewhere in his program without seriously damaging other program areas, which themselves are of high priority in interpreting the results of carcinogenicity tests and their relevance to man.

Newell and Peters indirectly criticize Saffiotti for a reluctance to delegate tasks to contractors. "I feel these things can be done without direct control by active scientists," remarks Newell of Saffiotti's general approach to management. "I believe that you can go out and buy expertise and you can get good expertise. With the in vivo tests the protocols are so well developed that it is sort of cookbook," Peters says.

Saffiotti rejects this attitude, believing that unless the contractors are rigorously supervised, the tests will not be done properly, and a sloppy test is a total waste of investment. "There is no such thing as cookbook stuff at any stage of the way," says Saffiotti. As the Kennedy hearings on commercial laboratory operations have shown (page 531, this issue), it is crucial to set high standards for contractor performance, Saffiotti contends. "In fact, it is almost axiomatic that if bioassays are used to claim a negative result for regulatory purposes, the sloppier the test the 'safer' will the product appear—unless one investigates the adequacy of the procedures used."

In a letter of resignation sent on 23 April, Saffiotti ascribes the backlog in publishing the test results to a "tragic policy" by the NCI of failing to provide his bioassay team with sufficient staff. Reassignment and disruptions in his present staff appear likely "to lead to further delays in the publication of well-docu-

mented evidence of cancer hazards," he says in his letter. "I cannot accept any longer a situation which in fact deprives the regulatory agencies, industry, labor, consumers and the scientific community of data of urgent public health value: it is *people* who are now exposed to toxic agents and who are not protected because the necessary support was not provided in time."

Sloppy Tests

Saffiotti considers that he has had "at best only a few opportunities to discuss and participate in major policy decisions at the Institute level." Rauscher, he says, has received advice from his program "at second or third hand." The problem, as he sees it, is layers of bureaucracy separating the NCI director from his scientific experts. "There is a huge bureaucracy in the front office—some 200 people, few of whom are active scientists—and our own division director has built up a small layer of people in his front office," Saffiotti says. "Essentially the direct involvement in research stops at our level and all the rest is bureaucratic overhead. This may be the inevitable result of the very rapid growth of the NCI's budget, but the fact is that it is so."

The observation is serious, if true, not least because one of the principal arguments for giving the cancer institute greater autonomy within the National Institutes of Health was to free it from encumbering layers of bureaucracy. Rauscher, however, says he has never refused to see Saffiotti. Peters observes that he is the only person between Saffiotti and the NCI director, and that he has a larger program but smaller staff than any other division in the NCI.

One apparent example of the exclusion of experts from their proper role is that of a proposed interagency committee on the assessment of carcinogens. Peters has nominated himself as the NCI member. Asked if Saffiotti wouldn't be better qualified, Peters says no, because the committee is a broad-based policy group. But the chairman of the committee, Roy Albert of the Environmental Protection Agency, says that the committee will be a technical group making scientific judgments. Asked why Peters was a member, Albert said, "It does look peculiar that he is on it without being an expert in carcinogenesis or having that background, but I view it as only on the basis of setting up a channel to the NCI's experts such as [H.F.] Kraybill and Saffiotti." Peters has designated Kraybill as an alternate on the committee.

The bureaucracy's actions are not always accountable to peer review by outside scientists, Saffiotti believes. For example, the division of cancer cause and prevention has disbanded the peer review group it used to have. Thus although there are peer review groups at the program level, the decisions taken at divisional level, such as on allocation between the three programs (carcinogenesis, virology, and epidemiology) are not subject to direct peer review. Peters says the divisional level peer review group was disbanded because it did not make sense to have experts in one program area reviewing work done in another. According to Rauscher, however, "Active researchers have probably never had a greater input to the NCI—we have 62 advisory committees and I don't know of a single recommendation from them over which I have control which I did not implement."

An attempt to test the opinion of scientists in the chemical carcinogenesis field and on the NCI advisory board produced general praise of Saffiotti's program—"He has done as well as anybody could possibly do," says one of the outside advisers to his program. There seems to be a general reluctance to comment on the specifics of the issue, about which most people expressed ignorance. Members of the NCI advisory board were unaware even of the way in which the NCI's 79 staff positions had been distributed. "Internal NCI affairs are very complex, and outsiders comment on them at their peril because there are so many political issues involved," observes Nobel laureate Howard Temin of the University of Wisconsin.

Saffiotti's complaints may or may not be fully justified, but his resignation has at the least drawn attention to what he regards as a critical shortage of support for the carcinogenesis program.

—NICHOLAS WADE

Clinical Labs: Bills Aimed at Correcting "Massive" Problems

In medical practice today, physicians and patients rely increasingly on the results of laboratory tests to tell them what is wrong. And what is wrong, it seems, in an appalling number of cases, is the test itself. It is almost impossible to get accurate data on the quality of work performed in the 64,000 to 94,000 clinical laboratories in the United States (no one is sure exactly how many there are), but the Senate has evidence that "from 7 to 26 percent of all lab tests may be in error."* Considering the number of laboratory tests performed in any year, that is a lot of error.

According to figures from the Senate subcommittee on health, chaired by Edward M. Kennedy (D–Mass.), 4½ billion lab tests were conducted in this country in 1975; that comes out to 12 million a day. By the end of the year, the nation's total bill for laboratory tests hit $12 billion, which is roughly equal to 10 percent of the entire cost of health care for that year. Reports by the Senate's Special Committee on Aging, which conducted an investigation of Medicare fraud in the lab business, the Senate's subcommittee on health, and others reveal that problems with clinical laboratories are "massive and widespread." As Kennedy has said, "Clinical laboratories perform inadequately and constitute a threat to the public health."

In the Senate, Kennedy and Jacob K. Javits (R–N.Y.) have sought a remedy through the Clinical Laboratories Improvement Act of 1975, which is likely to go to the floor for action soon. Representative Paul G. Rogers (D–Fla.) has introduced similar, though not identical, legislation in the House. And the Administration, which is perfectly willing to concede there is a problem, is trying to block legislative action on the grounds that there already exist adequate powers to regulate clinical laboratories and that the government is now going to use them. But Congress is not going to hold its breath until that happens.

Nine years ago, Senator Javits in-

*"Fraud and abuse among clinical laboratories," a staff report prepared for the U.S. Senate's Special Committee on Aging, 1976.