

PRECLINICAL AND CLINICAL TESTING BY  
THE PHARMACEUTICAL INDUSTRY, 1976

---

---

JOINT HEARINGS  
BEFORE THE  
SUBCOMMITTEE ON HEALTH  
OF THE  
COMMITTEE ON  
LABOR AND PUBLIC WELFARE  
AND THE  
SUBCOMMITTEE ON  
ADMINISTRATIVE PRACTICE AND PROCEDURE  
OF THE  
COMMITTEE ON THE JUDICIARY  
UNITED STATES SENATE  
NINETY-FOURTH CONGRESS  
SECOND SESSION  
ON  
EXAMINATION OF THE PROCESS OF DRUG TESTING AND  
FDA'S ROLE IN THE REGULATION AND CONDITIONS  
UNDER WHICH SUCH TESTING IS CARRIED OUT

---

PART II

---

JANUARY 20 AND 22, 1976

---

Printed for the use of the Committee on Labor and Public Welfare  
and the Committee on the Judiciary

U.S. GOVERNMENT PRINTING OFFICE  
WASHINGTON : 1976

7-144 O

5521-74

5541-82

## COMMITTEE ON LABOR AND PUBLIC WELFARE

HARRISON A. WILLIAMS, Jr., New Jersey, *Chairman*

JENNINGS RANDOLPH, West Virginia	JACOB K. JAVITS, New York
CLAIBORNE PELL, Rhode Island	RICHARD S. SCHWEIKER, Pennsylvania
EDWARD M. KENNEDY, Massachusetts	ROBERT TAFT, Jr., Ohio
GAYLORD NELSON, Wisconsin	J. GLENN BEALL, Jr., Maryland
WALTER F. MONDALE, Minnesota	ROBERT T. STAFFORD, Vermont
THOMAS F. EAGLETON, Missouri	PAUL LAXALT, Nevada
ALAN CRANSTON, California	
WILLIAM D. HATHAWAY, Maine	
JOHN A. DURKIN, New Hampshire	

DONALD ELISBURG, *General Counsel*  
MARJORIE M. WHITTAKER, *Chief Clerk*  
JAY B. CUTLER, *Minority Counsel*

## SUBCOMMITTEE ON HEALTH

EDWARD M. KENNEDY, Massachusetts, *Chairman*

HARRISON A. WILLIAMS, Jr., New Jersey	RICHARD S. SCHWEIKER, Pennsylvania
GAYLORD NELSON, Wisconsin	JACOB K. JAVITS, New York
THOMAS F. EAGLETON, Missouri	J. GLENN BEALL, Jr., Maryland
ALAN CRANSTON, California	ROBERT TAFT, Jr., Ohio
CLAIBORNE PELL, Rhode Island	ROBERT T. STAFFORD, Vermont
WALTER F. MONDALE, Minnesota	PAUL LAXALT, Nevada
WILLIAM D. HATHAWAY, Maine	
JOHN A. DURKIN, New Hampshire	

LEROY G. GOLDMAN, *Professional Staff Member*  
JAY B. CUTLER, *Minority Counsel*

## COMMITTEE ON THE JUDICIARY

JAMES O. EASTLAND, Mississippi, *Chairman*

JOHN L. MCCLELLAN, Arkansas	ROMAN L. HRUSKA, Nebraska
PHILIP A. HART, Michigan	HIRAM L. FONG, Hawaii
EDWARD M. KENNEDY, Massachusetts	HUGH SCOTT, Pennsylvania
BIRCH BAYH, Indiana	STROM THURMOND, South Carolina
QUENTIN N. BURDICK, North Dakota	CHARLES McC. MATHIAS, Jr., Maryland
ROBERT C. BYRD, West Virginia	WILLIAM L. SCOTT, Virginia
JOHN V. TUNNEY, California	
JAMES ABOUREZK, South Dakota	

## SUBCOMMITTEE ON ADMINISTRATIVE PRACTICE AND PROCEDURE

EDWARD M. KENNEDY, Massachusetts, *Chairman*

PHILIP A. HART, Michigan	STROM THURMOND, South Carolina
BIRCH BAYH, Indiana	CHARLES McC. MATHIAS, Jr., Maryland
QUENTIN N. BURDICK, North Dakota	HUGH SCOTT, Pennsylvania
JOHN V. TUNNEY, California	

THOMAS M. SUBMAN, *Counsel*  
WALTER J. SHERIDAN, *Chief Investigator*  
STEPHEN L. JONES, *Minority Counsel*

# CONTENTS

## CHRONOLOGICAL LIST OF WITNESSES

TUESDAY, JANUARY 20, 1976

Schmidt, Alexander M., M.D., Commissioner, Food and Drug Administration, accompanied by Richard A. Merrill, General Counsel, FDA; Richard Crout, M.D., Director, Bureau of Drugs; Robert C. Wetherell, Jr., Director, Office of Legislative Services; Carlton Sharp, Searle Investigation Task Force; William D'Aguzzo, Ph. D., Assistant Director for Pharmacology-Toxicology, Office of Scientific Evaluation; M. Adrian Gross, D.V.M., Assistant Director for Scientific Coordination; Phillip Brodsky, Consumer Safety Officer, Inspection Branch, Philadelphia District; and Richard Ronk, Bureau of Foods, Director, Division of Food and Color Additives, a panel.....	Page 4
Quarles, John R. Jr., Deputy Administrator, U.S. Environmental Protection Agency (EPA); and Frank J. Rauscher, Jr., Ph. D., Director, National Cancer Institute, National Cancer Program, Public Health Service, Department of Health, Education, and Welfare.....	131
Searle, Daniel C., chief executive officer, G. D. Searle & Co., accompanied by Dr. James A. Buzard, vice president for operations; and Tomas M. Russell, Esq., Sidley & Austin.....	162

THURSDAY, JANUARY 22, 1976

Ahart, Gregory J., Director, Manpower and Welfare Division, U.S. General Accounting Office, accompanied by Albert B. Jojokian, Assistant Director, Manpower and Welfare Division; Carl D. McClure, supervisory auditor, Manpower and Welfare Division; and Charles Coughenour, supervisory auditor, Detroit regional office.....	224
Kass, Edward H., M.D., Ph. D., William Ellery Channing, professor of medicine, Harvard Medical School, and director, Channing Laboratory, Boston City Hospital, Boston, Mass., accompanied by Leslie G. Ford, M.D., Bureau of Quality Assurance, Department of Health, Education, and Welfare; and Calvin F. Kay, M.D., deputy executive vice president, American College of Physicians.....	278

### STATEMENTS

Ahart, Gregory J., Director, Manpower and Welfare Division, U.S. General Accounting Office, accompanied by Albert B. Jojokian, Assistant Director, Manpower and Welfare Division; Carl D. McClure, supervisory auditor, Manpower and Welfare Division; and Charles Coughenour, supervisory auditor, Detroit regional office.....	224
Prepared statement.....	270
Environmental Protection Agency, John R. Quarles, Jr., Deputy Administrator, prepared statement.....	136
G. D. Searle & Co., Daniel C. Searle, chief executive director, prepared statement.....	173
Inter-Society Committee on Antimicrobial Drug Usage (ISCAMU), Edward H. Kass, cochairman, prepared statement.....	258
Kass, Edward H., M.D., Ph. D., William Ellery Channing, professor of medicine, Harvard Medical School, and director, Channing Laboratory, Boston City Hospital, Boston, Mass., accompanied by Leslie G. Ford, M.D., Bureau of Quality Assurance, Department of Health, Education, and Welfare; and Calvin F. Kay, M.D., deputy executive vice president, American College of Physicians.....	278
Prepared statement.....	258
National Cancer Institute, Frank J. Rauscher, Jr., Ph. D., Director, prepared statement.....	147
Quarles, John R. Jr., Deputy Administrator, U.S. Environmental Protection Agency (EPA); and Frank J. Rauscher, Jr., Ph. D., Director, National Cancer Institute, National Cancer Program, Public Health Service, Department of Health, Education, and Welfare.....	131
Prepared statement.....	128

Schmidt, Alexander M., M.D., Commissioner, Food and Drug Administration, accompanied by Richard A. Merrill, General Counsel, FDA; Richard Crot, M.D., Director, Bureau of Drugs; Robert C. Wetherell, Jr., Director, Office of Legislative Services; Carlton Sharp, Searle Investigation Task Force; William D'Aguzzano, Ph. D., Assistant Director for Pharmacology-Toxicology, Office of Scientific Evaluation; M. Adrian Gross, D.V.M., Assistant Director for Scientific Coordination; Phillip Brodsky, Consumer Safety Officer, Inspection Branch, Philadelphia District; and Richard Ronk, Bureau of Foods, Director, Division of Food and Color Additives, a panel.....	Page 4
Prepared statement.....	50
Summary of prepared statement.....	111
Searle, Daniel C., chief executive officer, G. D. Searle & Co., accompanied by Dr. James A. Buzard, vice president for operations; and Thomas M. Russell, Esq., Sidley & Austin.....	162
Prepared statement.....	173
Supplementary statement.....	281
U.S. General Accounting Office, Gregory J. Ahart, Director, Manpower and Welfare Division, prepared statement.....	360
Veisical Chemical Corp., Robert Morris, president, prepared statement (with attachment).....	232

## ADDITIONAL INFORMATION

Articles, publications, etc.:	
Aspartame (A.P.M.) safety studies, memorandum from Mr. Perkins, consultant, FDA, to J. R. Pendry, G. Searle Co., August 4, 1975.....	16
Comparative pathology of chlorinated hydrocarbons, histopathologic findings in livers of rats fed diets containing Dieldrin and Aldrin, report of ad hoc committee, March 23, 1974.....	220
Effects of feeding diets containing a mixture of Heptachlor and Heptachlor Epoxide to female rats for 2 years, from the Kettering Laboratory, University of Cincinnati, Cincinnati, Ohio, January 28, 1966.....	244
Food and Drug Administration additional budget request for fiscal year 1977.....	8
FDA's list of animals by letter and number involving a variety of different tests.....	21
Food and drug sweetener strategy, memorandum from Mr. Helling to Dr. Buzard, Dr. Chien, Dr. Jenkins, Dr. Moe, and Mr. O'Bleness, December 28, 1970.....	17
Problems Involving the Effectiveness of Vaccines, report to the Subcommittee on Executive Reorganization and Government Research, Committee on Government Operations, U.S. Senate, March 28, 1972.....	392
Short treatise on the mammary gland (breast); its importance in pre-clinical and clinical drug safety evaluations and in maintaining any given drug on the market, memorandum from Dr. McConnell to Dr. Moe, December 16, 1971.....	10
Status report on investigation, memorandum from Searle Investigation Task Force to Searle Investigation Steering Committee, December 8, 1975.....	24
Testing of vaccines at Fort Detrick, Md.....	356
Use of Antimicrobial Agents in General Hospitals in Pennsylvania, Contract No. ASH-74-282-111B (amended 8/1/75 pursuant to authority of U.S.C. 252(a)(10)).....	430
Veisical Chemical Corp., et al., re suspension of Chlordane and Heptachlor, from the U.S. Environmental Protection Agency, transcript of proceedings, October 14, 1975.....	271
Communications to:	
Kennedy, Hon. Edward M., chairman, Subcommittee on Health, from: Nielsen, Donald P., president, Hazleton Laboratories America, Inc., Vienna, Va., January 30, 1976 (with enclosure).....	276
Searle, Daniel C., chief executive officer, G.D. Searle & Co., Chicago, Ill., February 13, 1976.....	279
Sloan, M. J., Ph. D., manager, regulatory affairs, Shell Chemical Co., San Ramon, Calif., February 8, 1976 (with enclosure).....	214
Schmidt, Dr. Alexander M., Commissioner, Food and Drug Administration, from James A. Buzard, G. D. Searle & Co., January 7, 1975 (with enclosure).....	183
Thurmond, Hon. Strom, a U.S. Senator from the State of South Carolina, from D. C. Searle, chief executive officer, Searle Laboratories, Chicago, Ill., February 13, 1976 (with enclosures).....	312

PRECLINICAL AND CLINICAL TESTING BY THE  
PHARMACEUTICAL INDUSTRY, 1976

TUESDAY, JANUARY 20, 1976

U.S. SENATE,  
SUBCOMMITTEE ON HEALTH OF THE  
COMMITTEE ON LABOR AND PUBLIC WELFARE;  
SUBCOMMITTEE ON ADMINISTRATIVE PRACTICE  
AND PROCEDURE OF THE COMMITTEE ON THE JUDICIARY,  
Washington, D.C.

The subcommittees met, pursuant to notice, at 9:30 a.m., in room 4232 Dirksen Senate Office Building, Senator Edward M. Kennedy (chairman of the subcommittees), presiding.

Present: Senators Kennedy, Nelson, Javits, and Beall.

Committee staff present: Jay B. Cutler, minority counsel.

Senator KENNEDY. We will come to order.

It is now 6 months since witnesses from the Food and Drug Administration appeared before these subcommittees to raise serious questions about the integrity of the scientific data submitted to the FDA by the G. D. Searle Co.

The issues raised in July are at the very heart of the regulatory process. Although judgments in that process may reasonably differ, all judgments are made from the same foundation—scientific data.

If the integrity of that data is questioned, then the whole regulatory process is questioned. If the data are proven false and misleading, then the regulatory decisions may be tragically wrong. Accurate science is the best protection the American people have from an unsafe and ineffective drug supply.

Inaccurate science, sloppy science, fraudulent science—these are the greatest threats to the health and safety of the American people. Whether the science is wrong because of clerical error, or because of poor technique, or because of incompetence, or because of criminal negligence, is less important than the fact that it is wrong.

For if it is wrong, and if, as in this case, the FDA did not—indeed, under current practice, could not—know it was wrong, then the protective regulatory barrier between a potentially dangerous drug and the patient is removed.

In the last 6 months, at these subcommittees' insistence, the FDA has reviewed the raw animal data for seven of G. D. Searle's products. Their task force has done an exhaustive job. The Commissioner of the FDA has taken a close personal interest. He has kept these subcommittees fully informed.

He and his staff are to be commended. I would like to single out for special praise Dr. Adrian Gross, whose professional compe-

That is why these problems are so serious. That is why scientific integrity must be maintained. That is why these subcommittees will insist that the Environmental Protection Agency, the National Cancer Institute, the Consumer Product Safety Commission, and every other relevant Government agency do what the FDA is going to do—review the quality of their animal work; identify any problems; propose solutions and report back to these subcommittees. There is no activity which should receive a higher priority.

Senator Javits?

Senator JAVITS. Mr. Chairman, at the July 10, 1975, hearings, we heard dramatic, disquieting testimony respecting the integrity of the testing of new drugs by the G. D. Searle & Co.

This testimony regarding the validity of the data which supports applications to test and market a new product caused Senator Schweiker, the chairman and myself great concern. We recommended that the Food and Drug Administration Commissioner, Dr. Schmidt, initiate a full and complete investigation of the integrity of the animal data submitted by G. D. Searle & Co. to the FDA in support of the safety of its products.

While the final FDA task force report is not completed, I have reviewed the preliminary information presented in Commissioner Schmidt's prepared statement. It is deeply disturbing. The deficiencies exposed raise critically serious questions about G. D. Searle & Co. and the whole pharmaceutical industry, of which Searle is an important member.

The public has no choice but to be deeply concerned about whether the regulatory process—which requires that the private enterprise system must act in good faith—is, in fact, operating in the public interest.

This critical question is raised—to his great credit and commendation—by the Commissioner himself. In the draft of his prepared statement dated January 18, 1976, he states:

Are the problems found at Searle unique or industrywide? Do these findings cast doubt on the safety of our foods and drugs?

The first question—whether these problems are industrywide—we are not able to answer definitely at this point. Prudence dictates, however, that we assume the presence of an industrywide problem until proven otherwise, and our plans for the future are based on his assumption.

Dr. Schmidt may be assured that he will have my strong continued support in finding the answer to this critical question. The health and safety of the American people demand an effective FDA regulatory process.

The Commissioner's conclusion which would "require new Federal resources and be greatly aided by new legislative authorities" is an important first step in this direction. I urge him—as I did at the July 10 hearing—"to be an initiator in terms of recommendations to us, as to what ought to be done respecting the regulatory process."

Senator KENNEDY. We welcome back to this committee Dr. Alexander Schmidt, Commissioner of the Food and Drug Administration, who has appeared before this committee on a number of different occasions. We always find these appearances useful and helpful to us.

As I indicated in my opening statement, we want to express, from the committee's point of view, and I suppose from an individual's

tence, integrity and unyielding dedication to his job are primarily responsible for uncovering this problem.

There is much talk about bureaucrats these days—99 percent of it derogatory. I think the American people should know about Dr. Adrian Gross and the thousands of others like him in every branch of this government who work hard and well in service to the people of this country.

I have personally reviewed the findings of the FDA task force. I believe they cast doubt upon the integrity of the research program at Searle. Whether the programs at Searle are shared by other pharmaceutical companies is not clear. But I do not believe we can take that chance. These subcommittees will insist that the FDA immediately institute a program to review the work of the other drug manufacturers.

We stand ready to work to provide FDA with the resources it needs to do the job. We intend to monitor this activity and we expect the Commissioner to report back to us expeditiously.

We must know the extent of this problem, and we must know quickly. We cannot have millions of Americans taking drugs which were deemed safe on the basis of unsound scientific data. These subcommittees will press the FDA until the facts are known, the problems are identified and solutions are developed.

The importance of animal data to the health policies of this government extends far beyond the Food and Drug Administration. The National Cancer Institute, the Environmental Protection Agency, the Consumer Product Safety Commission—all depend upon animal data. This Nation is committed to an all-out effort to conquer cancer, to clean up the air and water, to detect and eliminate potential carcinogens from the environment. We cannot have these efforts undermined by unacceptable science.

The importance of research in these areas cannot be underestimated. Every day every American is exposed to a variety of potentially deadly substances. The exposure may be in the form of a drug taken over many years; it may be artificial colorings in meat; or pollutants in the air and water or additives in our food.

We must know what the long-term cumulative effects of these exposures are likely to be. Animal studies are an integral part of this research. If a drug causes cancer in animals, it is a serious warning. Physicians must be alerted. Use of the drug must be restricted. Patients must be informed of the potential risk.

Because so many of us are exposed to so many of these agents, the potential for extensive harm is great. We can get an idea of the problem from the DES tragedy; DES-caused cancer occurred years after the exposure, and in the offspring of the mothers taking the drug.

There is additional evidence from the current estrogen controversy. Used since the late 1930's, we are now told that Premarin is directly linked to cancer of the uterus. How many women are at risk? How many people would be at risk if best-selling drugs are shown to cause cancer 20 years after they are first taken?

There is a long list of potential killers. There is little conclusive scientific evidence now. If only a small minority of these potential problems occur, the results could be catastrophic.

point of view, the great appreciation that we have for the cooperation that you and your staff have provided this committee and for the diligence in the work that you have done in the review of this particular matter.

We look forward to your testimony here this morning. If you will introduce your colleagues; they are familiar. I think everybody has been here before; but if not, introduce those who have not been here.

STATEMENT OF ALEXANDER M. SCHMIDT, M.D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION; ACCOMPANIED BY RICHARD A. MERRILL, GENERAL COUNSEL, FDA; RICHARD CROUT, M.D., DIRECTOR, BUREAU OF DRUGS; ROBERT C. WETHERELL, JR., DIRECTOR, OFFICE OF LEGISLATIVE SERVICES; CARLTON SHARP, SEARLE INVESTIGATION TASK FORCE; WILLIAM D'AGUANNO, PH.D., ASSISTANT DIRECTOR FOR PHARMACOLOGY-TOXICOLOGY, OFFICE OF SCIENTIFIC EVALUATION; M. ADRIAN GROSS, D.V.M., ASSISTANT DIRECTOR FOR SCIENTIFIC COORDINATION; PHILLIP BRODSKY, CONSUMER SAFETY OFFICER, INSPECTION BRANCH, PHILADELPHIA DISTRICT; AND RICHARD RONK, BUREAU OF FOODS, DIRECTOR, DIVISION OF FOOD AND COLOR ADDITIVES, A PANEL

Dr. SCHMIDT. I think all but one or two have been here.

On my immediate left is Mr. Richard Merrill, our General Counsel; on my right is Dr. Richard Crout, Director of the Bureau of Drugs; on his right is Mr. Carlton Sharp, who has headed our investigative task force; on his right is Dr. William D'Aguzzano from our Office of Scientific Evaluation; then at the end of the table is Dr. Adrian Gross, who is our Assistant Director for Scientific Coordination. On my far left, your far right, is Mr. Phillip Brodsky, who is a consumer safety officer from our Philadelphia district, who served as the field director for the recently completed investigations at Searle.

We are here this morning to discuss the quality of animal testing—

Senator KENNEDY. As I understand it, you have a more extensive and lengthy statement.

Dr. SCHMIDT. Yes, sir. I have a rather detailed and lengthy narrative statement which I would like to include for the record.

Senator KENNEDY. It will be included in the record at the conclusion of your testimony.

You have another statement that is quite extensive and complete and which I think is terribly important. There will be a few areas where I will ask you to elaborate, but we will see if we can continue the flow of the testimony.

Dr. SCHMIDT. Thank you.

With your permission, I will supply the long statement for the record and proceed with the shorter statement.

We are here this morning to discuss the quality of animal testing being conducted on products regulated under the Federal Food, Drug

and Cosmetic Act, and specifically, our investigation of Searle Laboratories.

The Federal Food, Drug, and Cosmetic Act imposed on manufacturers the burden of demonstrating that their products meet the safety requirements of the law. The Food and Drug Administration [FDA] conducts relatively little toxicology testing of its own and no clinical testing. Instead, we prescribe the type and extent of testing we believe necessary for a determination of safety and then review the data submitted by manufacturers to determine whether they meet these requirements. Thus, we require that all new drugs and food additives undergo extensive testing in animals to determine the fundamental toxicity profile of the compound, and particularly to determine whether they have any teratogenic potential, and to determine carcinogenicity whenever there is the likelihood of chronic exposure of humans.

Animal studies of human drugs are of particular importance in determining whether new products can safely be tested in humans to assess their potential therapeutic effect.

Because of the importance of animal toxicology data to our decisions, it is essential that these studies be technically complete, be conducted according to sound protocols, and be scrupulously controlled for quality.

At the July 10, 1975, hearing of these subcommittees, we described the questions that had arisen regarding the integrity of animal data submitted to us by the G. D. Searle Co. relating to the drugs, Flagyl and Aldactone.

From these preliminary investigations, we concluded that an in-depth study of the experimental animal operations of the firm was very much in order; and as you will recall from the hearing of July 10, 1975, we indicated we would investigate the animal studies submitted in support of Searle drugs marketed since 1968. Subsequently, we decided to include other Searle products, including the investigational drug Norpace and the food additive Aspartame.

To conduct the Searle investigation efficiently and expeditiously, an FDA task force was created in August 1975, to review the company's practices in conducting animal experiments, in analyzing the data, and in submitting this information to the FDA; determine whether any practices of Searle in conducting animal research are in violation of any laws; and recommend appropriate corrective action based upon the findings of the investigation.

The task force promptly prepared a plan for the investigation, and established investigating teams of well-qualified drug investigators and pharmacologists.

The task force then arranged for the review of all Searle submissions of animal data since July 1, 1968, to identify the laboratory which performed the study, its purpose, the animal species involved, duration, and the route of administration of the product; established criteria for selecting the products and studies to be investigated intensively; initiated an in-house review of the selected studies; on October 6, 1975, initiated the onsite phase of the investigation, with

teams going to Searle and Hazleton Laboratories simultaneously. The enormous task for reviewing the intimate details, involving literally millions of pieces of data, of the 25 selected studies continued until December 18, 1975.

During this period, the investigation teams generally spent 3 out of every 4 weeks at Searle or Hazleton, often working 18 hours a day.

I would emphasize, because I think the point will come up later, the tremendous amount of work that has been accomplished in reviewing these 25 studies.

At the present time, the task force, with the assistance of a group of pharmacologists, is still analyzing the data contained in the draft reports. Therefore, the findings that I will describe shortly must be considered as subject to some modification.

In addition, the distinct possibility of legal action growing out of this investigation requires that some of our findings be described only in general terms.

Once the final review has been completed, any necessary followup on the completed studies will be undertaken and the task force will prepare a final report and recommendations. In the meantime, consultation will soon begin with the Department of Justice to assure that all relevant material is available to them when we reach final decisions on the appropriateness of regulatory action.

Senator KENNEDY. Are you sending the material there?

Dr. SCHMIDT. Yes, sir. We have decided, as we proceed through the final stages of our evaluation, that we would consult continuously with the Justice Department, and have been in contact with them and will continue to work with them in the evaluation of our findings.

Now, in regard to the investigation in general, we found, regretably, that the required attention to detail in conducting these animal studies is sometimes lacking. For some time, we have been concerned about the absence of industrywide standards, and the lack of a systematic Federal inspection program for toxicology laboratories. The importance and complexity of these studies are by themselves sufficient reason to recommend such a program. But in addition, there is now growing evidence of significant quality-control problems in these laboratories. Some of this evidence comes from our Searle investigation.

Senator KENNEDY. Do you believe there to be a general problem throughout the industry?

Dr. SCHMIDT. We believe at this time, on the basis of the limited evidence that we have from our own inspections, that there is some degree of a generalized problem. We are not yet in a position to describe factually and in detail the extent of an industrywide problem.

We believe that certainly not all laboratories, not all pharmaceutical firms have had all of the problems that we found at Searle. But we do believe that there are general and industrywide problems in conducting, in planning and carrying out and reporting these kinds of studies.

One of the things that we intend to do is to systematically sample the universe of drug firms, contract laboratories and others to deter-

mine factually what kind of problems exist and how extensive they are.

We intend to do this in conjunction with other Federal agencies.

Senator KENNEDY. I understand you will make some specific recommendations on this point a little later in your testimony; but as I understand from this point here, you are sufficiently concerned about this particular issue from an industrywide position that you are going to take steps to review industrywide the animal studies which, in this particular case with regard to Searle, you found to be so bothersome, troublesome and distressing?

Dr. SCHMIDT. In general; yes.

I think that we simply do not have the resources to evaluate all animal studies of all contract laboratories and pharmaceutical houses. What we intend to do is to set up scientific and systematic sampling of the universe of the people who do these studies. That will tell us whether there is a serious industrywide problem or whether the laboratories and firms are distributed on a curve, some better than others, which is what I would suspect.

Senator KENNEDY. We recognize that you cannot do all these various drugs; but there is no reason that you cannot test at least the ones which are being used to the greatest degree.

Dr. SCHMIDT. In selecting the drugs that we looked at in the Searle Lab, we set up some interesting criteria for selecting drugs to look at which pose the most risk to individuals taking them. This is described in my longer statement.

We would use the same kind of a screening process for selecting those drugs and those pharmaceutical houses for a serious look at their animal work.

Senator KENNEDY. But as a potential problem, you are sufficiently concerned and distressed, based upon what you found in this particular investigation as well as its relationship to other submissions, by other companies; that you believe it is of prime importance in terms of the role of your agency as well as others?

Dr. SCHMIDT. Yes, sir. Our priorities are first to complete very quickly the Searle investigation and then immediately to move on to survey other firms and contract laboratories.

Senator JAVITS. Mr. Chairman, would you allow me to break in at this point just for a request?

I would suggest, Commissioner, that to assist our Chairman who is so ably carrying this on as is our ranking member, Senator Schweiker, and myself and others, that at the same time that you come to us with your report, you request the additional resources which will enable you to do what has to be done.

I am very alarmed by your testimony, obviously; but even more so by the fact that on so critical a matter, the resources of the FDA should be insufficient to do what the public interest may require.

So if you would be kind enough, Commissioner, to ask us for what you need, it would be our duty to do our best to get it in time rather than just to have you feel limited because you do not have the resources.

