5.

CURRENT ASSESSMENT ACTIVITIES

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CURRENT ASSESSMENT ACTIVITIES

This chapter describes Federal Government and private sector activities for assessing the efficacy and safety of medical technologies. It is not an evaluation of the performance of the agencies, except where such performance is affected by the presence or absence of policies relating to efficacy and safety.

Federal Government Activities

FOOD AND DRUG ADMINISTRATION

The Food and Drug Administration (FDA) of the Department of Health, Education, and Welfare (HEW) is one of the principal Federal regulatory agencies designed to protect the health of the American public. Over the past two decades, FDA's responsibilities in the protection of health have increased significantly. In 1970, there were only three product-oriented bureaus: foods, drugs, and veterinary medicine. Subsequently, the agency has taken on responsibilities encompassing a broad range of medical technologies, such as X-ray equipment and other radiation-emitting medical and consumer devices, blood banks, vaccines and allergenic, organ transplants, and other biological products.

The growth in the agency's jurisdiction has been accompanied by a concomitant increase in its budget and staff. Between 1954 and 1977, FDA's budget grew from $5.5 million to $250 million; the staff increased from less than 1,000 to 7,300 (123,240). FDA's FY 1977 budget represented approximately 4 percent of the Public Health Service budget and 40 percent of total Federal outlays for consumer protection.

The specific role FDA envisions for itself is regulating the transfer of medical technologies from the level of medical researcher to the level of health practitioner and consumer. The agency particularly emphasizes regulation in those areas where consumers cannot make reasonably informed judgments. These regulatory responsibilities give FDA one of the most direct Federal roles in assuring the efficacy and safety of two major classes of medical technologies: drugs and medical devices.

Prescription Drugs: Statutory Authority

FDA is responsible for implementing the Food, Drug, and Cosmetic Act of 1938. This Act mandates Federal regulation of all drugs. As the Act's principal enforcer, FDA is required to approve all new drugs before they are marketed. Such approval is contingent upon the demonstrated efficacy and safety of a new drug.

The requirement that the efficacy of a new drug be demonstrated before approval was added to the Act by amendment in 1962. Previously, the 1938 Act restricted FDA's

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review to the safety of drugs. Therefore, the fact that a particular drug was not shown to be efficacious could not, in most cases, serve as the basis for disapproval of its marketing application.

Two statements from the 1962 amendments form the basis for FDA's definition of efficacy. According to the legislation, the FDA Commissioner must refuse approval of a drug marketing application if, after notice and opportunity for hearing, he or she determines that "there is lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof. . ."* Substantial evidence is defined in the Act as: "evidence consisting of adequate and well-controlled investigations, including clinical investigations, . . . on the basis of which it could fairly and responsibly be concluded. . . that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. " No distinction is made either in the Act or its implementing regulations between the terms efficacy and effectiveness.

Safety is assessed as a separate factor from efficacy. FDA must weigh the relative benefits and risks associated with the use of the drug, and the drug may enter the market only when the benefits derived from its use clearly outweigh the risks.

Prescription Drugs: Regulation

All drugs which are not already on the market, or generally recognized by experts as safe and effective under prescribed conditions of use, must undergo premarket review. This process begins with the submission of a "new drug application" (NDA) by the manufacturer to FDA. Minimally, NDAs must contain a full report both of the investigations conducted to determine a drug's efficacy and safety, and the methods, facilities, and controls used in its manufacture, processing, and packaging. In addition, labeling samples to be used for the drug must be included. FDA must either approve the application or notify the applicant of an opportunity for a hearing within 180 days after an application is filed. During the 180-day period, FDA attempts to determine if the therapeutic benefits of the new drug justify its potential risks.

FDA may provide exemptions from the NDA process to those intending to use the drug solely for investigational purposes. However, a "Notice of Claimed Investigational Exemption for a New Drug" (IND) must be filed by anyone planning to conduct research involving the use of new drugs by human beings. An IND must contain chemical, manufacturing, and control information, results of animal studies, and a description of the protocol for the clinical study, including information about the investigator and facilities for the study. If FDA does not prohibit the research within 30 days following the IND filing, the research may commence.

Medical Devices: Statutory Authority

FDA was first provided authority to regulate medical devices in the Food, Drug, and Cosmetic Act of 1938. This Act extended FDA control over foods and drugs and gave FDA new powers with regard to cosmetics and medical devices. Under the Act the FDA had to prove that a product was in fact dangerous or fraudulent before any action could be taken to remove the product from the market.

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*These amendments also required drug firms to demonstrate the efficaciousness of all drugs marketed between 1938 and 1962.

The development and use of medical devices has expanded greatly since the passage of the 1938 Act. As a result of the dynamic growth of the industry, more complex, sophisticated, and technologically challenging products were being developed that had the potential to cause serious patient injury or even death. In response to some of the possible dangers inherent in such growth, Congress enacted the Medical Device Amendments of 1976, which bestowed FDA with significant new authority to ensure the safety and efficacy of medical devices. These amendments were enacted primarily to provide regulatory safeguards commensurate with the potential consumer risks associated with the use of increasingly sophisticated medical devices. Accordingly, they require evaluations of efficacy and safety to be made "weighing any probable benefit to health from use of the device against any risk of injury or illness from such use. " To achieve such evaluations, Congress both expanded FDA's operative definition of medical devices and required classification of all devices into one of three regulatory categories, differentiated according to the extent of control necessary to ensure their efficacy and safety.

As defined in the amendments, a medical device is any health care product that does not achieve any of its principal intended purposes either by chemical action within or on the body, or by being metabolized. Examples of devices included in this definition are optical prescription lenses and frames, hearing aids, intrauterine devices, surgical instruments, cardiac pacemakers, and CT scanners. The definition also applies to *in vitro* diagnostic products, including those that were previously defined and regulated as drugs. It is estimated that there are more than 8,000 products currently on the market that conform to the expanded definition.

FDA designed its system of classification and regulatory controls to prevent unnecessary regulation of device manufacturers while simultaneously providing maximum protection to consumers. Devices placed in the Class I category are subject only to general controls which include premarket notification, adherence to good manufacturing practices, and recordkeeping requirements. * *Class II* medical devices must meet FDA's performance standards which may relate to their construction, components, ingredients, and properties. A manufacturer must seek premarket approval of a medical device both when general controls would not ensure its safety and efficacy and when there is insufficient information available to develop performance standards. Premarket approval is the overriding regulatory requirement for Class III devices. Devices that are life sustaining, life supporting, or implanted into the body usually must be placed in the Class III category.

A manufacturer who develops a new device must notify FDA at least 90 days in advance of its placement on the market. During this 90-day period FDA determines the class in which the device belongs through regulations which require the manufacturer to supply: 1) proposed labels, advertising, and directions for use; 2) statements regarding the similarity to or difference from products already on the market; and 3) descriptions of how a device complies with existing standards regulations.

Medical Devices: Regulation

Implementation of the 1976 Amendments began with the assignment of devices into the three regulatory categories. Nineteen panels were created to recommend classifications for a total of 3,500 generic categories of devices. Each panel was composed of seven voting members who were professionals with training and experience in the clinical, scientific, and engineering aspects of devices. One industry and one consumer represen-

'General controls apply to devices in all three categories.

tative served as nonvoting members on each panel. The panel reports, which were recently released and contained over 7,000 pages of documentation, provide both the recommended classification for each device reviewed, and evaluations of each generic category of devices. Approximately 37, 59, and 4 percent of the devices were recommended for placement in Classes I, II, and III, respectively (360).

Regulations pertaining to Class I devices (section 520(f) of the amendments) direct FDA to "prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacturing, packing, storage, and installation of a device conform to current good manufacturing practices (GMP). " FDA has published a proposed GMP regulation which applies to all devices, and is therefore known as the "umbrella" GMP. Failure to comply with the GMP renders a device "adulterated," and regulatory action can be initiated against the manufacturer.

Section 514 of the amendments authorized FDA to develop and promulgate performance standards for devices in *Class II*. Standards maybe developed by FDA or outside organizations. For example, contracts have been awarded to extramural organizations to develop standards for electrocardiographs (EKG), electromagnetic compatibility, electrosurgical devices, and infant incubators, among other devices. FDA may also adopt an existing standard as the mandatory one.

To review the adequacy of existing standards and to guide the development of new ones, FDA annually prepares a comprehensive list of current national and international standards activities for medical devices and diagnostic products. Criteria for such attributes as performance, sensitivity, accuracy, materials, safety, and durability are included in the standards listed. FDA works closely with voluntary standards organizations to review and possibly adopt some consensus standards already developed by these agencies.

As stated previously, devices classified into *Class III* are required to undergo a process of premarket approval. This process entails the submission of a premarket approval application. These applications are then referred to the appropriate classification panel for review and subsequent recommendation to FDA. The application must include, among other things, a summary presenting a sound case for approval and a review of all known data published that demonstrates the product's safety and efficacy. Following the panel's recommendation, FDA will approve or disapprove the application within 180 days of its receipt, unless a longer period of review time is agreed to by FDA and the applicant. Manufacturers of pre-enactment *Class III* devices (any device in commercial distribution before May 1979) have 30 months after final classification to develop data demonstrating the efficacy and safety of such devices before FDA can require the submission of a premarket approval application.

All testing of devices that involves the use of human subjects will be required to follow FDA's regulations governing the investigational use of devices, after these regulations are published in final form and become effective.

NATIONAL INSTITUTES OF HEALTH

The principal biomedical research agency within the Federal Government operating under HEW, is the National Institutes of Health (NIH). It was established in the immediate post-Second World War years both to consolidate the Government's medical research activities and to conduct, encourage, and support medical research and develop-

ment. NIH currently receives approximately two-thirds of all Federal dollars allocated to biomedical research, although more than a dozen other Federal agencies also conduct such research. NIH provided an estimated $2.24 billion in biomedical research support in 1977; this amount represents approximately 40 percent of all moneys expended for medical research in the United States during that year (260).

Biomedical research conducted by NIH includes studies of drugs, devices, and medical and surgical procedures. These studies usually are accomplished through grant and contract awards to academic and other research institutions. However, NIH generally does not synthesize the evidence regarding efficacy and safety gained from these studies.

Statutory Authority

Section 301 of the Public Health Service Act provides NIH with its basic research authority. This section of the Act authorizes the Surgeon General of the Public Health Service (the parent agency of NIH) to encourage and assist "research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man. " In addition to the general statutory authority provided by the Public Health Service Act, 8 of the 11 institutes comprising NIH have specific legislative mandates to fulfill particular research functions for certain categories of disease. For example, the National Cancer Institute (NCI) and the National Heart, Lung, and Blood Institute (NHLBI), the two largest components of NIH, are governed by statutes which include requirements to engage in demonstration and control programs relevant to those disease categories.

Specific references to efficacy or effectiveness do not appear in any of the NIH legislative authorities. However, NIH concern regarding the efficacy and safety of medical technologies can be assumed from the general language it uses to describe its mission: 1) advancing knowledge and understanding of the normal and pathological processes of the human body, and 2) developing ways in which the providers of medical care can safely and effectively intervene to prevent, treat, or cure diseases and disabilities.

Clinical Trial Support

Clinical trials provide the basis for the testing and orderly application of fundamental research knowledge prior to its general introduction into the health care system. These trials assist in preventing the premature introduction of new diagnostic and treatment hypotheses into general practice. Often, such trials are the only methods used for testing and evaluating the safety and efficacy of new diagnostic and treatment developments.

NIH investment in both the support and conduct of clinical trials has increased substantially in recent years. Four out of the eleven institutes* nearly tripled their total obligations for major clinical trials between 1971 and 1974. In FY 1975 alone, NIH provided approximately $110 million to support clinical trials; this figure represents 5 percent of the total NIH budget for FY 1975. Completion of these trials was estimated to cost another $345 million.

Tables 2, 3, and 4, on the following pages illustrate NIH support for clinical trials during FY 1975. Table 2 delineates clinical trial investment both by institute and by type

● The four institutes were the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute of Neurological and Communicative Disorders and Stroke; and the National Eye Institute.

Table 2.—National Institutes of Health 1975 Inventory of Clinical Trials

Amount of NIH Support for Clinical Trials Active in Fiscal Year 1975 by Institute and Type of Support

(in millions of dollars)

NIH Institute*	Extramural support: Grant	Contract **	Grant & contract	Total	Intramural support ***	Amount of support
NEI	$0.8	$2.1	—	$2.9	$0.2	$3.1
NHLBI	4.3	37.8	0.1	42.2	0.5	42,7
NIAID	1.3	1.5	—	2.8	0.3	3.1
NIAMDD	1.8	0.9	—	2.7	0.7	3.4
NCI	14.0	7.5	2.6	24.1	2.5	26.5
NICHHD	1.3	1.8	0.2	3.4	0.5	3.9
NIDR	0.8	0.2	—	1.1	0.7	1.7
NINCDS	0.8	0.6	—	1.4	2.0	3.4
NIGMS	0.1	—	—	0.1	—	0.1
Total	$25.1	$52.6	$2.9	$80.6	$7.3	$87.8

*Names of Institues: NEI = National Eye Institute; NHLBI = National Heart, Lung, and Blood Institute; NIAID = National Institute of Allergy and Infectious Disease; NIAMDD = National Institute of Arthritis, Metabolism, and Digestives Diseases; NCI = National Cancer Institute; NICHHD = National Institute of Child Health and Human Development; NIDR = National Institute of Dental Research; NINCDS = National Institute of Neurological and Communicative Disorders and Stroke; NIGMS = National Institute of General Medical Sciences.

**Contract includes interagency agreements without intramural support.

***Intramural support includes intramural support in combination with interagency agreements.

Table 3.—National Institutes of Health 1975 Inventory of Clinical Trials

Number of Clinical Trials Supported by NIH in Fiscal Year 1975 by Institute and Type of Support

NIH Institute	Number of trials supported extramurally: Grant	Contract *	Grant & contract	Total	Number of trials conducted intramurally**	Total number of trials
NEI	13	2	—	15	5	20
NHLBI	6	16	1	23	3	26
NIAID	78	21	—	99	10	109
NIAMDD	29	14	—	43	6	49
NCI	253	66	48	367	38	405
NICHHD	24	12	1	37	4	41
NIDR	25	6	—	31	13	44
NINCDS	13	8	—	21	38	59
NIGMS	2	·	—	2	—	2
Total	443	145	50	638	117	755

*Contract includes interagency agreements without intramural support.

**Intramural support includes intramural support in combination with interagency agreements.

Table 4.—National Institutes of Health 1975 Inventory of Clinical Trials

Number of and Amount of Support for NIH Supported Clinical Trials Active in Fiscal Year 1975 **by Institute and Type of Intervention**

(in millions of dollars)

NIH Institute	Total trials supported in FY 1975		Type of intervention					
			Therapeutic		Prophylactic		Diagnostic	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
NEI	20	$3.1	11	$2.4	—	—	9	$0.7
NHLBI . . .	26	42.7	16	27.0	9	$14.6	1	1.2
NIAID	109	3.1	53	1.2	29	1.5	27	0.5
NIAMDD .	49	3.4	45	3.3	2	0.0	2	0.0
NCI	405	26.5	372	23.6	12	1.3	21	1.6
NICHHD. .	41	3.9	11	0.6	21	2.7	9	0.6
NIDR	44	1.7	16	0.7	17	0.7	11	0.3
NINCDS. .	59	3.4	49	3.0	5	0.3	5	0.2
NIGMS. . .	2	0.1	2	0.1	—	—	—	—
Total. . .	755	$87.8	575	$61.8	95	$20.9	85	$5.1

of expenditure, Table 3 indicates the number of clinical trials conducted by each institute, As evidenced in this table, the average expenditure per trial ranged widely from $1.6 million for NHLBI to $28,000 for NIAID and NIGMS.

Table 4 outlines expenditures by three functions of technology: therapeutic, prophylactic, or diagnostic. Clinical trials investigating therapeutic technologies were predominant in 1975. Supplemental information provided by NIH indicates that a total of 535 trials were conducted to test drugs either in isolation or in combination with another type of technology. Four hundred of these trials tested drugs in isolation. More than **300** trials tested cancer chemotherapies; only **25** evaluated surgical procedures. Eighty-five trials examined such diagnostic technologies as CT scanning for brain tumors and fluorescent scanning in thyroid disease. However, few clinical trials examined the efficacy of screening or early diagnosis. Trials of primary prevention were quite rare.

NIH interest in conducting and disseminating the results of clinical trials continues to grow. For example, a summary of clinical trials under NIH support is assembled annually, which is divided according to type of trial and level of expenditure. In addition, the agency has established an NIH Clinical Trials Committee to coordinate work in the areas of design, taxonomy, and trial monitoring strategies. NIH held a major conference in the fall of 1977 for persons engaged in this type of research to impart information recently generated about clinical trial methodology.

Consensus Development

According to NIH, the present process for diffusion of medical technologies "leads to a situation in which the practicing community at large is not prepared to react promptly and in the best informed state to rapid advances in technology. . . . While the Food and Drug Administration has stringent requirements for the safety and efficacy of drugs, biologics, and devices, many procedures existing in current medical practice and new interventions entering the medical arena and adopted by practitioners are not amenable to such regulatory action and require more critical appraisal of effectiveness" **(382).** Although there have been many situations where a clinical trial has firmly established the efficacy and safety of a particular medical technology, there are other situations in which

the results of a clinical trial have been equivocal. Also, in some cases controlled trials may indicate that a technology is of limited benefit. Thus, the technology is efficacious but the value of this limited efficacy must be evaluated by other techniques besides the controlled trials. In some cases clinical trials may be prohibitively expensive. In other cases trials may pose difficult ethical and moral considerations. In such cases clinical experience can bean important factor in determining what use should be made of the technology.

Due to both the inherent limitations in clinical trials and the need for improved methods of disseminating research information, NIH initiated a process for developing a consensus among representative experts regarding the proper role of a given medical technology. NIH entitled that process "technical consensus development. " Representatives of various segments of the medical community are asked to agree on five issues: the clinical significance of the new findings; the adequacy of efforts to validate efficacy and safety; the need to identify cost, ethical, or other social impacts as points for caution; the need for feasibility demonstrations in community settings; and whether research results are phrased for easy understanding; and acceptance by health practitioners (381).

Hypertension was one of the first areas in which technical consensus development was applied (see chapter 3, case 12). Initially, NIH appointed a Committee on Detection, Evaluation, and Treatment of High Blood Pressure, which included individuals representing a wide range of professional groups, including the American Medical Association, the American College of Cardiology, the American College of Physicians, and the American Heart Association. This committee developed detailed recommendations on the management of hypertension, which included diagnostic procedures and a listing of effective therapies. Because the committee reflected such a broad base of interested parties, and therefore had great credibility, the recommendations were widely adopted.

A second major example of consensus development application at NIH was the 1977 Meeting on Breast Cancer Screening (see chapter 3, case 4). The meeting was held to coincide with the completion of a review of the Breast Cancer Detection Demonstration Project (BCDDP), which involved periodic screening of large numbers of women for breast cancer using clinical history, physical examination, mammography and thermography. Critics had questioned whether the use of radiation (by mammography) to detect cancers might not subsequently trigger development of malignancies.

NIH convened a 16-member panel composed of scientists, epidemiologists, and physicians from various disciplines, including radiology, medical oncology, surgery, and general medicine. Representatives of the clergy, legal profession, and lay public were also asked to participate on the panel.

Subsequent to the gathering of evidence, the panel developed 12 recommendations regarding the risks, benefits, and ethical considerations involved in the BCDDP, in particular, and screening, in general. The recommendations ranged from specific suggestions for determining which risk groups should continue to undergo periodic screening and the appropriate radiation dose, to general recommendations regarding the need for additional research in particular subject areas,

In January 1978, NIH established the position of Associate Director for Medical Applications of Research as a response to the success of the consensus development process. The Associate Director and staff work with individual institutes to increase awareness of each institute's activities in consensus development. Additionally, they coordinate consensus development efforts which involve a number of institutes simultaneously. This office has recently developed guidelines for methods to be utilized in: 1) the identification

of new knowledge pertinent to health care, 2) consensus development conferences, and 3) the dissemination of research information. Other technical consensus conferences are being planned by the Associate Director in conjunction with the other institutes. Table 5 lists conferences being coordinated during 1978 and 1979.

Table 5.—Consensus Development Conferences
National Institutes of Health

Time	Institute	Title	Format
May 1978	NCI	Medical Aspects of Asbestos	Conference
June 1978	NIEHS	International Cadmium Conference	Conference
June 1978	NIDR	Dental Implants	International conference
June 1978	NIH Nutrition Coordinating Committee	Nutrition in the Eighties	Panels and formal presentations; 2 days
June 1978	NCI	Mass Screening for Colo-Rectal Cancer	Cconference of European & American scientists
July 1978	NIA	Treatable Brain Diseases in the Elderly	2-Day meeting
July 1978	NINCDS	Indications for Tonsillectomy and Adenoidectomy	Advisory group
August or October 1978	NHLBI	Early Hospital Discharge of Patients with Uncomplicated Myocardial Infarction	Panel
September 1978	NIAID	Availability of Insect Sting Kits to Non physicians	Panel
September 1978	NICHHD	Antenatal Diagnosis	Panel
November 1978	NIGMS	Supportive Therapy in Burn Care	2-Day workshop
Summer 1978	DRS (BEIB)	The Use of Microprocessor-Based, 'Intelligent, ' Machines in Patient Care	Workshops (series of 4)
December 1978	NIAMDD	Intestinal Bypass Surgery in Treatment of Massive Obesity	Panel
1978	NIEHS	Standards for Laboratory Use of Toxic Substances Posing a Potential Risk	Panel
1978	NIA	Postmenopausal Estrogen Treatment	Preliminary planning meeting
1978	NCI	Mass Screening for Lung Cancer	Conference
1978	NCI	Rehabilitation for Cancer Patients	Conference
1978	NIEHS	Toxicological Evaluation of Hair Dyes	Workshop
1978	NCI	Health Education Workshop	Workshop
1978	NCI (ION, NIA)	Palliative Care of the Terminally Ill	Conference
1979	NHLBI	Prophylactic Use of Low Dose Heparin in the Prevention of Venous Thrombosis and Pulmonary Embolism	Panel
1979	NHLBI	Use of Extracorporeal Membrane Oxygenator (ECMO) in the Treatment of Adult Respiratory Failure	Public meeting
1979	NEI	Photocoagulation Therapy for Diabetic Retinopathy	Panel
1979	NIEHS	Validation of Short-Term Tests as Predictors of Carcinogenic and Mutagenic Activity	Conference
1979	Interagency Committee or New Therapies for Pain and Discomfort	Pain and Its Relief	Panels and formal presentations; 2 days

Source: Information furnished by staff of the Associate Director for Medical Applications of Research, NIH.

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

The Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), another agency within HEW, incorporates programs of basic and applied research, service, and training, which are relevant to the understanding and treatment of mental illness, drug abuse, and alcoholism, in its three component institutes: the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH). ADAMHA has conducted research to establish the safety and efficacy of medical technologies since the 1950's. In 1975, however, ADAMHA established Treatment Assessment Research (TAR) as a separate research category, specifically designed to study the relative safety and efficacy of various substances and procedures applied to human subjects. This research includes prospective clinical trials, case reports, retrospective surveys, and reanalysis of early data. The three ADAMHA institutes provided $19 million to support TAR in FY 1975.

TAR was identified as a major agency priority in 1978 (359). To assist TAR, a work group was established with the following overall aims:

1. To develop a plan that will assess the current state of TAR and develop research programs in selected high-priority areas,
2. To advise the Administrator and the institute Directors on priorities for the areas of treatment assessment studies that are important to public health and are feasible within the next 2 years,
3. To develop a long-term plan that will keep the agency abreast of both methodological and substantive developments in order that the institutes' programs can rapidly reflect these developments and changing needs.

Tables 6 and 7 outline the FY 1975 ADAMHA investment in TAR. Table 6 delineates TAR investment by institute and by type of support. Table 7 presents both the number of studies and amount of support by type of intervention. As evidenced in table 6, NIMH programs are the most developed, particularly in the evaluation of the safety and efficacy of drugs used to treat the mentally ill. The $1.5 million figure listed for NIMH under the "grant and intramural" support largely represents that agency's program in collaborative clinical trials. Examples of such trials include the study of hyperbaric oxygen treatment for cognitive defects in the elderly (see chapter 3, case 17) and a study of intensive social casework and neuroleptic drugs in treatment of outpatient schizophrenia (166, 142).

Table 7 indicates that, similar to NIH clinical trials, most research moneys are allocated to therapeutic interventions (82 percent). A smaller portion of money is devoted to diagnostic interventions (12 percent). Only 6 percent of the funds went to study prophylaxis in FY 1975.

HEALTH SERVICES ADMINISTRATION

Several components of the Health Services Administration (HSA), also an HEW agency, conduct assessments of efficacy and safety and support other activities closely related to such assessment. The Indian Health Service and Public Health Service (PHS) hospitals and clinics are extensively involved in testing computer applications to improve the handling of medical information. In addition, PHS hospitals and clinics are involved in clinical drug trials and other research studies supported by both intramural funds and

Table 6.—Alcohol, Drug Abuse, and Mental Health Administration 1975 Inventory of Treatment Assessment Research

Number of and Amount of Support for ADAM HA Supported Treatment Assessment Research Projects Active in Fiscal Year 1975 by Institute and Type of Intervention

(in millions of dollars)

ADAM HA Institute"	Total TAR'S supported in FY 1975		Type of intervention					
			Therapeutic		Prophylactic		Diagnostic	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
NIAAA . . .	8	$0.4	8	$0.4	–	–	–	
NIDA	52	5.3	49	5.1	–	—	3	$0-1
NIMH	237	13.6	187	10.2	18	$1.2	32	2.1
Total. . .	297	$19.3	244	$15.8	18	$1.2	35	$2.2

•Institute names: NIAAA = National Institute on Alcohol Abuse and Alcoholism; NIDA = National Institute on Drug Abuse; NIMH = National Institute of Mental Health.

Table 7.—Alcohol, Drug Abuse, and Mental Health Administration 1975 Inventory of Treatment Assessment Research

Amount of ADAM HA Support for Treatment Assessment Research Projects Active in Fiscal Year 1975 by Institute and Type of Support

(in millions of dollars)

ADAM HA Institute	Extramural support				Intramural support	Amount of support
	Grant	Contract	Grant & intramural	Total		
NIAAA.	$ 0.4	—	—	$ 0.4	—	$0.4
NIDA	4.0	$1.3	—	5.3	—	5.3
NIMH	10.3	0.0	$1.6	11.9	$1.7	13.6
Total	$14.7	$1.3	$1.6	$17.6	$1.7	$19.3

competitively acquired extramural funds. The nation's largest effort in studying Hansen's disease is conducted by PHS Hospital in Carville, La., with considerable technology development and new technology transfer in the area of treatment of insensitive limbs. The Indian Health Service also has been involved in the evaluation of space technology developed by the National Aeronautics and Space Administration (NASA) for application to remote rural health facilities.

NATIONAL CENTER FOR HEALTH SERVICES RESEARCH

The National Center for Health Services Research (NCHSR) is a component agency of the Office of the Assistant Secretary for Health of HEW. It was established by Public Law **93-353,** the Health Services Research, Health Statistics, and Medical Libraries Act of 1974. NCHSR is authorized to undertake a broad range of research documentation and to evaluate activities pertaining to nearly all aspects of health care delivery.

According to the agency, the "assessments supported by NCHSR are best characterized in a general sense as cost-benefit/cost-effectiveness studies' '(369). These assessments often take place during demonstrations, whereby a technological innovation is studied in the context of the actual health care delivery setting. A mixture of efficacy, safety, effectiveness, and cost information is often developed during these types of assessments. NCHSR has demonstrated, and sometimes developed, a number of technologies, many of which are computer based. The agency also has supported an investigation, conducted by the American College of Radiology, of the efficacy of various X-ray procedures. "Technical consensus" techniques similar to those of NIH are sometimes used by the Center. For example, it sponsored an American College of Cardiology conference and report, *Optimal Electrocardiography* (371).

OFFICE OF HEALTH PRACTICE ASSESSMENT

The Office of Health Practice Assessment (OHPA) is located within the Office of the Assistant Secretary for Health, HEW. OHPA is responsible for providing coverage recommendations to the Social Security Administration (SSA) when questions arise regarding reimbursement coverage under Medicare for new services, devices, or procedures.* OHPA only synthesizes existing information on the efficacy and safety of a given technology; it does not conduct new studies. The agency collects available data and translates that information into recommendations to Medicare regarding coverage. Final authority for deciding issues of Medicare coverage resides in the Health Care Financing Administration (HCFA).

OHPA recommendations are based on evidence in four areas: efficacy, safety, stage of development (i. e., the progression of a technology from the experimental stage to full clinical application), and acceptance by the medical community. Upon receipt of a coverage question, the OHPA staff members conduct literature reviews and contact relevant experts both inside and outside the Government. The opinions of these consultants are contained in a memorandum of recommendation to Medicare that cites relevant evidence regarding the four criteria listed above. The opinion provided by OHPA affects only Medicare; Medicaid coverage is decided by the States. To date, recommendations have been developed for only a minority of the technologies Medicare reimburses.

PHS and HCFA have had several discussions about the four areas of evidence (criteria for coverage). Both agencies agree that cost-effectiveness and cost-benefit considerations should be included in coverage determinations. Some modification of the criteria is actively being considered (319).

A second technology-related activity that OHPA conducts is the Medical Practice Information Demonstration Project. This Project addresses a two-fold problem: that medical practice, including the use of medical technology, is based on information that ranges from hard scientific knowledge to judgment, speculation, and assumption; and that the differences in validity of these sources of medical practice information are not explicit. The Medical Practice Information Demonstration Project is an attempt both to develop and test the feasibility of a technique designed to elicit consensus from recog-

*Before the reorganization of HEW in 1977, reimbursement questions were referred to the Public Health Service's Bureau of Quality Assurance. That Bureau is now the Health Standards and Quality Bureau of the Health Care Financing Administration.

nized experts in a particular field of medical practice regarding the epidemiology, diagnosis, therapy, and economics of a disease entity, and to identify and validate the most authoritative scientific data supporting those opinions. The information derived from such a technique is expected to have these results:

1. Those conclusions about a disease entity or medical technology that rest on a valid information base can be put to immediate use in making regulatory and reimbursement decisions and in quality assurance programs;
2. Those conclusions and assumptions that are unsupportable or rest on an invalid base will help set priorities for biomedical and health services research;
3. The entire profile of validity from well-documented, scientifically supportable knowledge to mere assumptions will find immediate application in medical education.

HEALTH STANDARDS AND QUALITY BUREAU

The Health Standards and Quality Bureau (HSQB) is part of HCFA, HEW. The Bureau is composed of three distinct programs: Professional Standards Review Organization (PSRO), End Stage Renal Disease (ESRD), and Standards/Certification. The most significant of these programs is the PSRO, which is designed to assure that rendered services are medically necessary, consistent with professionally recognized standards, and delivered at an appropriate level of care. It is responsible for reviewing the provision of health services under the federally financed programs of the Social Security Act, i.e., Medicare, Medicaid, and Title V. PSRO medical necessity review determinations are used as conditions for the payment or denial of claims under Medicare and Medicaid.

The PSRO program provides a mechanism for developing consensus regarding the appropriate use of particular medical technologies through the criteria and standards development process. Each PSRO is responsible for developing its own criteria and standards. These standards are based on local patterns of medical practice. The National Professional Standards Review Council may adopt exemplary norms, standards, and criteria, and distribute them to PSROs for their adoption and use. Any locally developed norms, criteria, or standards of care that differ significantly from those developed by the National Council may be disapproved by it.

While the National Council has provided general guidance to the PSROs and sent actual criteria sets to PSROs for use, these have not been officially adopted, and therefore, are used only as technical assistance. HCFA has stated that the National Council will begin to adopt exemplary sets and review local PSRO sets to determine if they differ significantly. If the differences cannot be justified, the National Council is expected to disapprove the use of those norms, criteria, and standards by that PSRO.

Information for the criteria sets issued to date by the National Council was developed under contracts with such groups as the American Medical Association, the American College of Physicians, and various university hospitals. The primary purpose of the studies was to develop criteria on medical necessity for hospitalization for different disease categories. However, some of the criteria sets include indications for the effective use of drugs, devices, and procedures.

OTHER FEDERAL PROGRAMS

Only selected Federal programs involved in evaluations of efficacy and safety of medical technologies have been described. However, more than a dozen Federal agencies conduct or support biomedical research, some of which involve testing for efficacy or safety. Two agencies that conduct such testing are covered below: the Veterans Administration (VA) and the Department of Defense (DOD). Other agencies that conduct this type of research but are not covered in this report include NASA and the National Science Foundation (NSF).

Veterans Administration

The health programs administered by VA are designed to provide quality medical care to veterans. In order to furnish such care to veterans, VA spends approximately 80 percent of its health-related budget on direct provision of services. VA's Department of Medicine and Surgery runs the largest centrally directed patient care system in the United States and serves an eligible population of about 30 million. The authorizing statutes for VA do not include specific references to either efficacy or effectiveness. Nevertheless, the Department of Medicine and Surgery has promulgated regulations, manuals, and circulars related to the efficacy and safety of medical technologies and services.

VA (and DOD, see below) conducts a full range of technology activities, including research and development, validation assessment, transfer to practice, and dissemination of information. The Department of Medicine and Surgery has a Research and Development Division involved in basic medical research, clinical trials, health services research, and rehabilitative engineering. The FY **1976** budget for research and development was $96 million. All research is conducted within the VA system.

Clinical trials aimed at testing efficacy and safety can be funded either through the existing budgets of each facility or the Research and Development Division. In 1976, 24 multicenter cooperative studies were in progress. One of these studies tested various drug treatments for hypertension (see chapter 3, case 12). Other examples of such VA-sponsored studies include a trial of the efficacy of immune serum globulin for the prevention of post-transfusion hepatitis and a trial of methadyl acetate and methadone as maintenance treatment for heroin addiction (303,216).

Department of Defense

DOD operates a network of hospitals and clinics that are intended to provide health care for active-duty personnel and retired members of the uniformed services. The authorizing statutes covering the health programs in DOD do not mention efficacy or safety explicitly. The Assistant Secretary of Defense of Health Affairs, however, has responsibility for establishing uniform policies, standards, and procedures for medical care. Many directives and instructions establish criteria and standards for aspects of medical technology related to efficacy and safety, such as standards for the purchase of hardware. In addition, FDA performs the functions related to quality assurance of drugs, devices, and biologics procured by the Department.

DOD supports a considerable amount of health-related research. In 1976 alone, expenditures for health research totaled more than $114 million. DOD research and development activities are directed toward providing medical knowledge and expertise in those areas that primarily affect the military. These activities include clinical trials that

test the efficacy and safety of medical technologies. For example, DOD spends about $15 billion annually on the development and assessment of field medical care and evaluation systems (see chapter 3, case 5). In addition, approximately $40 million is spent each year to develop and assess new technologies to ensure troop readiness through disease prevention. A third area of DOD research and development activities involves the collection of scientific data for use in establishing safety criteria for exposure to hazards arising from military environments.

Private Sector Activities

The private sector supports many activities intended to evaluate the efficacy and safety of medical technologies. In addition, many Federal programs depend upon private sector facilities and personnel to produce much of the data used for evaluations of safety and efficacy. In fact, most federally financed clinical trials take place in private sector hospitals and clinics, many of which are university-affiliated.

The work of individual physicians or medical center research teams has resulted in a number of innovative medical and surgical procedures. Although there are few formal requirements that mandate new procedures be shown to be efficacious before their use, a substantial amount of testing is still conducted with or without Federal funds.

In addition, there are a number of indirect controls on the use of new technologies. Swazey **(332)** has identified four such controls: 1) professional training and socialization, 2) peer group controls, 3) design and conduct of clinical research, and 4) physician/patient or investigator/subject relationships.

Some professional associations have developed formal mechanisms for reviewing accumulated evidence regarding the proper use of a technology. * In late 1976, the Medical Practice Committee of the American College of Physicians recommended that the College "explore the feasibility of forming an organization to develop a mechanism for the systematic review of the efficacy of diagnostic and therapeutic procedures. " The American Academy of Pediatrics has developed recommendations on immunization practices. The American Public Health Association periodically compiles a list of effective preventive and therapeutic procedures for infectious diseases. The Council of Medical Specialty Societies, the American College of Surgeons, and the American College of Physicians have provided advice to the National Blue Shield on the efficacy of lumbodorsal sympathectomy, uterine suspension, and basal metabolic rate determinations—all questionable procedures for which Blue Shield was continuing to reimburse. The American Hospital Association and the American College of Radiology also have been involved in similar activities.

Professional associations are becoming increasingly involved in standards setting. Standards are seen as the means by which professionals, consumers, industry, and the Government can accept and communicate technical recommendations for certain characteristics of technologies. The usual mechanism for the development and approval of such standards is **a** multiorganization group that is composed of all relevant and affected disciplines and interests. The largest source of voluntary consensus standards is the American Society for Testing and Materials (ASTM). ASTM has promulgated voluntary standards

*In these reviews, distinctions between efficacy and effectiveness are hazy; however, they seem to emphasize effectiveness.

in several medical areas, including implantable devices and prosthetics. Standards approved by the members of ASTM are submitted to the American National Standards Institute (ANSI) for acceptance as the American National Standard. ANSI is a voluntary federation of more than 400 standards-writing bodies in the United States.

Another medical standards-setting group is the Association for the Advancement of Medical Instrumentation (AAMI). The Association, which represents 5,000 professional, corporate, and institutional members, provides a forum in which health care professionals, manufacturers of medical devices, and Government representatives can interact to develop standards that promote patient safety. This is accomplished by establishing basic performance and user information requirements. AAMI has committees operating in Ambulatory Monitoring, Autotransfusion, Human Engineering, and Otolaryngology, among other areas. These committees take into consideration all factors including technological and economic impacts relevant to the establishment of a reasonable level of safety and efficacy.

The Alliance for Engineering in Medicine and Biology also has assessed a number of medical technologies over the past few years, particularly in the area of ultrasonic diagnosis (41). The alliance usually does not conduct formal evaluations of the efficacy and safety of specific medical technologies. However, the alliance's assessments may increase practitioner awareness regarding the importance of considering both the type and validity of efficacy and safety information as it relates to technologies they use or plan to use. The alliance report on technology procurement in health care institutions (5) is an example of their efforts to provide practitioners and administrators with a process by which they can evaluate technologies.