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### The Specialized Information Services

#### THE DRUG LITERATURE PROGRAM

THE rapidly increasing literature about drugs in the years following World War II, the difficulty that researchers and physicians faced in obtaining data quickly on new medicines or on compounds tested as medicines, and the need for immediate warning about harmful drugs such as thalidomide, convinced Senator Hubert Humphrey, among others, that some means, perhaps a "National Drug Information Clearinghouse," was needed to collect, organize, and disseminate information on the subject. The director of Humphrey's subcommittee, visited the Library several times to discuss the matter with Director Rogers, Winifred Sewell and others. Deputy Director Adams spent much time at the Senate Office Building assisting the staff. In 1962 Humphrey asked Rogers to prepare a study on "The Nature and Magnitude of the Drug Literature." Sewell, who had been librarian of Wellcome Research Laboratories and Squibb Institute for Medical Research before coming to NLM, and was editor of *Unlisted Drugs*, wrote the report which emphasized the wide dispersion of material on drugs. Senator Humphrey, who had been a pharmacist before entering public life, used this report to buttress his proposal for the establishment of a special program in the Library to cope with the literature. The following year the President's Commission on Heart Disease, Cancer and Stroke also recommended that a National Drug Information Clearinghouse be established in NLM.<sup>1</sup>

Elsewhere the chief proponent for a drug information center was F. Ellis Kelsey of the Public Health Service. Kelsey, whose wife Frances O. Kelsey had helped keep thalidomide off the U.S. market, helped evolve a plan for the collection, organization, and dissemination of data on drugs. The plan advocated a division of work between the Food and Drug Administration, NIH, and the Library. The FDA would collect and disseminate information on unpublished work, NIH would support research and development to improve methods of handling chemical and biological data, and the Library would be responsible for published literature. Kelsey hoped to be placed in charge of the Library's program, with a large staff and considerable funds. But the amount of money and number of employees eventually allotted were considerably less than Kel-

sey expected. He died suddenly, and the leadership of the emerging program passed to others.

In the autumn of 1964 the Administration placed funds in the 1966 budget to establish a coordinated system for collecting, organizing, and disseminating information on drugs within the Department of Health, Education, and Welfare. One million dollars was allotted to the Library for development of a drug information clearinghouse, \$2.5 million was pinpointed for the Food and Drug Administration, and \$1.5 for NIH.

Informed of the approaching appropriation, Director Cummings placed Sewell in charge of the program. She drew up plans to extend the level of NLM's activities in drug literature, using approximately two-thirds of the appropriation for development of an in-house program and the remainder for grants and contracts. Six functions were anticipated: collection of all published literature on drugs; expansion of the number of publications covered by MEDLARS in the drug field, improvement of drug terminology in MESH so that articles on drugs could be indexed more accurately; expansion of reference and search services to researchers and to those engaged in regulatory work; providing of abstracts, translations, and bibliographies of articles about drugs; and research in communication of information on drugs to the biomedical community.

When funds became available Sewell began to engage a staff of pharmacologists, biochemists, medicinal chemists, and information specialists. She made arrangements for the Library to acquire more drug literature, particularly that supplied by card and microfilm services which had been previously excluded by the acquisition policy, and to subscribe to drug information services oriented primarily toward industry. Drug journals published throughout the world were examined to determine which should be added to the journals already being indexed for MEDLARS. Pharmacological terminology in MESH was improved so that drug articles could be indexed more precisely. Professional societies cooperated in the development of MESH by appointing panels of specialists to give advice on terminology. The American Hospital Formulary Service and the Library agreed to employ the same terminology insofar as feasible. At NLM's suggestion the Pharmaceutical Manufacturers' Association sent librarians to assist in the development of the Library's drug information program in exchange for access to MEDLARS, which at the time was available only to nonprofit organizations.

The DLP desired to index articles on drugs in a much more detailed manner than the usual medical article, so that regulatory agencies, researchers, pharmacists, physicians, and others who needed precise information about therapeutic use, pharmacologic action, and chemical composition of a compound could obtain it quickly. Moreover, it was important that the indexing be related to a specific chemical entity. At the time, Chemical Abstracts Service, under contract to National Science Foundation, was endeavoring to place on computer tape the registry numbers and detailed chemical descriptions of the millions

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of compounds indexed in *Chemical Abstracts*. Since the Cancer Chemotherapy National Service Center, the Food and Drug Administration, and the Drug Literature Program were all interested in a subset of this data base, the three groups agreed to extend the funding for this contract and have Chemical Abstracts Service register selected drugs and chemicals found in specific sources designated by the three groups. The tape, delivered in 1968, covered about 31,000 compounds in the fields of drugs, cosmetics, food additives, and other products. The data were also produced as *Desktop Analysis Tool for the Common Data Base* (six volumes), distributed by the National Technical Information Service.

It had been the intention of the Drug Literature Program to use the *Chemical Abstracts* data for synonym matching, to aid NLM indexing, and possibly to assign chemical class terms for MESH automatically. Computer programs for an auxiliary chemical module were partially written to enable this name matching process to proceed, but they were never completely tested and implemented owing to the redirection of emphasis during the development of MEDLARS II.

The Drug Literature Program's first bibliography was a monthly compilation of information on the adverse effects of drugs for the FDA. In July 1966 the DLP turned to MEDLARS to produce a pilot issue of *Toxicity Bibliography*, a list of reports on toxicity studies, adverse drug reactions, and poisoning in man and animals compiled from approximately 2,500 journals. After receiving suggestions for improvement of the bibliography from toxicologists, pharmacologists, pharmacists, and clinicians to whom the publication was sent for review, DLP modified the format and produced a second pilot issue in the spring of 1967. Following further modifications, the Library published the bibliography on a regular quarterly basis from 1968 until 1978.

## THE TOXICOLOGY INFORMATION PROGRAM

While the Drug Literature Program was evolving in the Library, the related subject of toxicology was receiving much publicity throughout the United States. Reports of harmful effects of chemicals in food, water, and the environment, along with the publication of articles and books such as Rachel Carson's *Silent Spring* aroused the public's interest and alarm. In 1964 James A. Shannon, Director of NIH, convened a group of NIH's pharmacologists to study the effects of environmental chemical contaminants upon life. The President's Science Advisory Committee, impressed by the NIH study, recommended the establishment of a National Toxicological Information System.<sup>2</sup> President Lyndon Johnson accepted the recommendation and assigned to the Department of Health, Education, and Welfare the responsibility for developing a computer-based file of toxicological information. From the Secretary of DHEW the responsibility passed down to the Surgeon General and finally to the Library.<sup>3</sup>

Director Cummings was concerned that NLM did not have the funds and specialized manpower to develop the large information service visualized by

his superiors in NIH, PHS, and DHEW, but he accepted the responsibility with the understanding that the Library would receive adequate resources. The Surgeon General transferred funds and four positions from his office to NLM to enable the program to begin. In December 1966 Cummings appointed Charles N. Rice, a chemist with industrial, academic, and governmental experience, to organize the program. Rice prepared a plan that was implemented after approval by a DHEW Departmental Toxicological Information Coordination Committee. Because the activities of the Drug Literature Program were similar to the new Toxicological Information Program, the former was placed under Rice's supervision on May 17, 1967. The name Specialized Information Services was coined to cover both units.

The DLP had focused primarily on acquiring, indexing, and compiling drug information. Since these activities overlapped ongoing library operations, some members of the staff were gradually transferred to sections of the Library responsible for these activities. Finally in 1970 the DLP was abolished leaving the Toxicology Information Program as the major element in the Specialized Information Services.

#### DEVELOPMENT OF THE TOXICOLOGY INFORMATION PROGRAM

Shortly after the Toxicology Information Program was established, Cummings requested the National Research Council-National Academy of Sciences to form an advisory committee, generally referred to as TIPCOM. Composed of several scientists prominent in toxicology and related fields, TIPCOM provided advice on the scope and priorities of the program.

Since the number of persons in TIP was small, much of the development, compiling, arranging, and other work had to be done by contractors, leaving the staff free to plan and manage. Rice negotiated contracts with University of Pittsburgh, University of Pennsylvania, and commercial firms to obtain several products, among them a directory of toxicology information resources in government agencies, industrial companies, and universities; a roster of experts in the various areas of toxicology; a data bank of user needs of toxicological information and data; and the design of a computerized data storage and on-line retrieval system for toxicology.

Director Cummings had expected to receive an increase in funds and positions each year to build the large program envisioned by the originators. However within a year or two it became apparent that the increase would not materialize:<sup>4</sup>

Fiscal Year	1967	'68	'69	'70	'71	'72	'73	'74	'75	'76
Anticipated funds	0.5	2.3	5.9							
Obligations, millions	0.051	0.586	1.380	1.240	1.311	1.315	1.533	1.747	1.881	1.9
Anticipated personnel	20	41	57							
Actual personnel	10	18	18	18	17	17	16	17	17	17

Therefore, the ongoing broad program covering many facets of toxicology could not be continued. The Library had to choose narrower but attainable goals that

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would allow TIP to function within its limited resources and to perform useful services as quickly as possible. Under Henry M. Kissman, a pharmaceutical chemist and information specialist, who arrived from the Food and Drug Administration in June 1970 to direct TIP, the primary objectives became: the operation of services to provide toxicological information and data to the scientific community; an increased collaboration with other government agencies which possessed data and information relevant to TIP's subject area or could use the services of TIP; and a continuation of the development of computerized toxicological data banks.

TIP provided services through publications, query-response, and the operation of a variety of on-line retrieval files and systems. The first of TIP's publications was a *Directory of Information on Resources in the United States: General Toxicology* (1969) prepared by the National Referral Center for Science and Technology at Library of Congress. Others included *Drug Interactions, an Annotated Bibliography with Selected Excerpts*, prepared by Paul de Haen, Inc.; *Index to the Report of the Secretary's Commission on Pesticides and their Relationship to Environmental Health*, prepared by Sharon Valley using a whole text data processing system; *Abstracts on Health Effects of Environmental Pollutants*, a monthly abstract journal initiated by TIP and published by Biosciences Information Service of Biological Abstracts.

The query-response service was brought about by an agreement between the Library and the Atomic Energy Commission to establish the Toxicology Information Response Center at the Oak Ridge National Laboratory. The center drew on the resources of the Library and Oak Ridge to provide answers to questions from users. The answer generally consisted of a bibliography compiled by computer searching of on-line files such as MEDLINE and hand searching of conventional sources like *Chemical Abstracts*, *Biological Abstracts*, and *Science Citation Index*.

Some of the queries received by the response center required considerable time and labor to answer. The Board of Regents approved Kissman's recommendation that searches completed within 2 hours be free, but those over 2 hours be charged \$15 for each additional hour, the money reverting to the Oak Ridge Laboratory to help offset the cost of the service. Some of the bibliographies compiled by the center were considered to be of such wide interest that they were published.

The Library's first whole text computerized search system was developed under the direction of Donald J. Hummel in TIP using *Health Aspects of Pesticides Abstracts Bulletin* and the facilities of a contractor, Mead Data Central Corp.. This served as a prototype for a nationwide retrieval service named TOXICON, developed with the aid of a contractor, Informatics, Inc.. TOXICON, an acronym for toxicology information conversational on-line network, was demonstrated by Specialized Information Services in April 1972. Regular service to subscribers was inaugurated on October 1 through the commercial Tymshare network. TOXICON at first contained citations from *Toxicity Bib-*



*Several of the publications provided to scientists working in the fields of pharmacology, toxicology, environmental pollution, and related disciplines by the Library's Specialized Information Services.*

*liography, Health Aspects of Pesticides Abstracts Bulletin, Chemical-Biological Activities, Abstracts on Health Effects of Environmental Pollutants, and a private collection of citations on pesticides compiled by Whalen J. Hayes. Later, citations from other files and services were introduced into the system. In 1973 the name TOXLINE, for toxicology on-line, replaced the name TOXICON. The following year the system, which had been operated by a contractor outside of the Library, was brought inside since NLM could now handle whole text search capabilities.*

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Following the successful establishment of TOXLINE, Bruno M. Vasta began to develop a companion file, the topline chemical dictionary, based upon the Chemical Abstracts Service registry numbers contained in TOXLINE. This file contained chemical identification data extracted and reformatted from data supplied by Chemical Abstracts Service, including generic and trivial names, registry numbers, and molecular formulas. These data, considered proprietary by CAS, required royalty payments based upon use. The file was tested as a prototype while running with TOXLINE in the National Aeronautics and Space Administration RECON satellite system and later was improved and renamed CHEMLINE when the service was offered directly from the Library.

In 1974 Michael Oxman and the TIP staff began to develop an on-line interactive computer-based data retrieval system that would provide access to chemical, physical, toxicologic, pharmacologic, use, and manufacturing data on hundreds of selected chemicals. The toxicology data bank, as the compilation was named, became available to U. S. subscribers of the Library's on-line computer services in November 1978.

TIP collaborated with Federal agencies and NIH Institutes in designing and developing other on-line bibliographic and data files. These included CANCERLIT and CANCERPROJ, with the staff of the National Cancer Institute; EPILEPSYLINE, with the staff of the National Institute of Neurological and Communicative Disorders and Stroke; and RTECS (registry of toxic effects of chemical substances) with the staff of the National Institute for Occupational Safety and Health.

The most widespread collaboration of the Specialized Information Services occurred in the Toxicology Information Subcommittee of the DHEW Committee to Coordinate Toxicology and Related Programs. This committee, organized by the Assistant Secretary for Health, was composed of representatives of 13 organizations within DHEW and liaison representatives from 13 other Federal agencies. Headed by Kissman, the information subcommittee drew a list of desirable projects to be undertaken by TIP. When the Assistant Secretary was able to obtain funds, TIP began the most urgent project. One of these was the laboratory animal data bank, LADB, a computerized repository of evaluated baseline data on many strains and species of animals such as mice, rats, rabbits, dogs, and monkeys used in research. Battelle Columbus Laboratory collected the data under contract from institutions throughout the United States, and the Library made the data available through an on-line retrieval and statistical analysis system designed for use by scientists, breeders, and managers of laboratory animal research. Formal training in computer retrieval logic was not necessary for use of this system. Another important project was a periodical that provided news of toxicity tests being carried out or considered by companies, universities, and government agencies. TIP collected the information and sent it to National Technical Information Service, which published it in a monthly bulletin titled *Tox-Tips* (from toxicology testing-in-progress). In a third project, reports about planned and ongoing research in toxicology were ex-

tracted from the data bank of the Smithsonian Science Information Exchange and published through NTIS as the monthly *Toxicology Research Projects Directory*.

In the 1960's when the Library was given responsibility for the Drug Literature and Toxicology Information programs, Director Cummings expected to receive authority to hire the relatively large number of professional employees and to receive the large annual appropriations envisioned by those who conceived the programs. Instead he was given authority to hire only a few scientists, and he received only a relatively small amount of money for the work. As a result, the Specialized Information Services had facilities and personnel to carry out only a fraction of possible worthwhile projects and at times was able to undertake an important proposal only by obtaining funds and borrowing positions from collaborators. The staff of the service demonstrated ingenuity and skill in accomplishing so much with limited resources.

#### Notes

<sup>1</sup> Information on the Drug Literature and Toxicology Information programs may be found in records of the Board of Regents, annual reports of the Library, *NLM News*, and articles published by members of the staff. Information was also obtained from Martin Cummings, Winifred Sewell, Charles Rice, George Cosmides, Henry Kissman, Donald Hummel, Sharon Valley, Arthur Wykes, and Donald Walker. 88th Cong., 1st sess., Committee Print, *Drug Literature. Report prepared for the Study of "Interagency Coordination in Drug Research and Regulation" by the Subcommittee on Reorganizations and Internal Organizations of the Senate Committee on Government Operations*

*A factual Survey on "The Nature and Magnitude of Drug Literature" by the National Library of Medicine*. Aug. 30, 1963.

<sup>2</sup> *Handling of Toxicological Information. A Report of the President's Science Advisory Committee* (Washington, The White House, 1966).

<sup>3</sup> Memo, Philip Lee, Asst. Sec. for Health and Scientific Affairs to Sec. DHEW, Sub. Development of Toxicological Information System, Jan. 31, 1967.

<sup>4</sup> Obligations and personnel are from annual reports of the Library. Anticipated funds and personnel are from memo, Surg. Gen. William Stewart to Sec. DHEW, sub: Development of toxicological information system, Dec. 12, 1966.