Chemical-Biological Coordination Center of the National Research Council (1952)

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HISTORY

The Coordination Center of the OSRD Insect Control Committee* (September 1944 - September 1945)

The Insect Control Committee of the Office of Scientific Research and Development (OSRD) was created in September, 1944, as one of the units of Division 5 (Division of Chemistry) of the Committee on Medical Research. It was charged with the responsibility of coordinating the work on insect and rodent control problems which was being carried out at the request of the Armed Forces with funds provided by the OSRD. This included: (1) a search for new insecticides and insect repellents; (2) a search for new rodenticides; (3) work on the formulation of insecticides and insect repellents; (4) fundamental studies of the mechanism of action of insecticides, insect repellents and rodenticides and (5) the development of improved methods for the dispersal of insecticides. The Insect Control Committee was composed of representatives of the Committee on Medical Research, the National Defense Research Committee and the Office of Field Service of the OSRD plus liaison representatives from the Army, Navy and other government agencies concerned with research on insect and rodent control problems.

The work of the Committee was divided among the following five subcommittees: Biology, Chemistry, Dispersal, Entomology and Rodent Control. Each subcommittee was provided with the full-time services of a technical aide who maintained close contact with the work of all of the subcommittees and with the pertinent work being carried out by the Committee on Medical Research, the National Defense Research Committee, the Army and Navy technical laboratories and their contractors, the Army Committee on Insect and Rodent Control, the Food and Drug Administration, the Bureau of Entomology and Plant Quarantine of the Department of Agriculture, the Fish and Wildlife Service of the Department of Interior, the National Institute of Health of the U.S. Public Health Service and the British Commonwealth Scientific Office. Frequent conferences were called by the various subcommittees which were attended by the leading investigators in the respective fields represented by the subcommittees plus representatives of the agencies with whom liaison was being maintained. The minutes of these meetings were widely distributed throughout the Armed Forces and to their contractors working on insect and rodent control problems.

The Coordination Center of the Insect Control Committee consisted of the above mentioned technical aides plus the necessary additional technical and clerical assistants serving under the direction of Dr. C. Chester Stock, Executive Secretary of the Insect Control Committee. This group had access to practically all of the data being accumulated on insect and rodent control, much of which was filed in the Center. At periodic intervals the information in specific fields was summarized by the Center's personnel and issued as Coordination Center Reviews. Nine of these reviews were published starting in December, 1944.

Early in 1945 it was decided that the Coordination Center would collect, abstract and index all reports and manuscripts concerned with insect and rodent control problems. These abstracts were issued in the form of Abstract Bulletins. These Bulletins contained abstracts of reports prepared for the Armed Forces by its contract investigators, abstracts of reports from the various Armed Forces technical laboratories and field stations, abstracts of reports from our Allies, as well as abstracts of the published literature concerning insect and rodent control matters. The contents of the Abstract Bulletins were divided into five groups corresponding to the subcommittees mentioned above. They were published biweekly starting February, 1945, and were issued in two series: Series A consisted of abstracts from Restricted and Open documents; Series B consisted of abstracts from Secret and Confidential documents. The publication of these series was completed in September, 1946. Three sets of indexes to the Series A and B Bulletins were also published and distributed.

* For a full account of the work of this Committee see Volume II, Chapter 35, of "Advances in Military Medicine", pp. 533-545. Little, Brown and Co., Boston, 1948.

In August, 1945, when the war was ended, it was decided to issue a new series of Abstract Bulletins which were classified as Open and which contained declassified data taken from the Series A and B Bulletins. The publication of the New Series Bulletins started in December, 1945, and was completed in February, 1947.

The Coordination Center of the National Research Council Insect Control Committee (September 1945 - July 1946)

Since the OSRD was established to serve only during the emergency it began to terminate its activities immediately after V-J day. Upon the combined request to the President of the National Academy of Sciences by the Director of the OSRD, the Secretaries of the War, Navy and Interior Departments and the Director of the Federal Security Agency, the Insect Control Committee was taken over by the National Research Council in September, 1945, so that its activities could be continued under peacetime conditions. Financial support was provided by the OSRD until June 30, 1946. Drs. Herbert Scoville, Jr., Richard A. Ormsbee and Raimon L. Beard served, successively, as Executive Secretary of the Committee during this period.

The Chemical-Biological Coordination Center of the National Research Council (July 1946 - date)

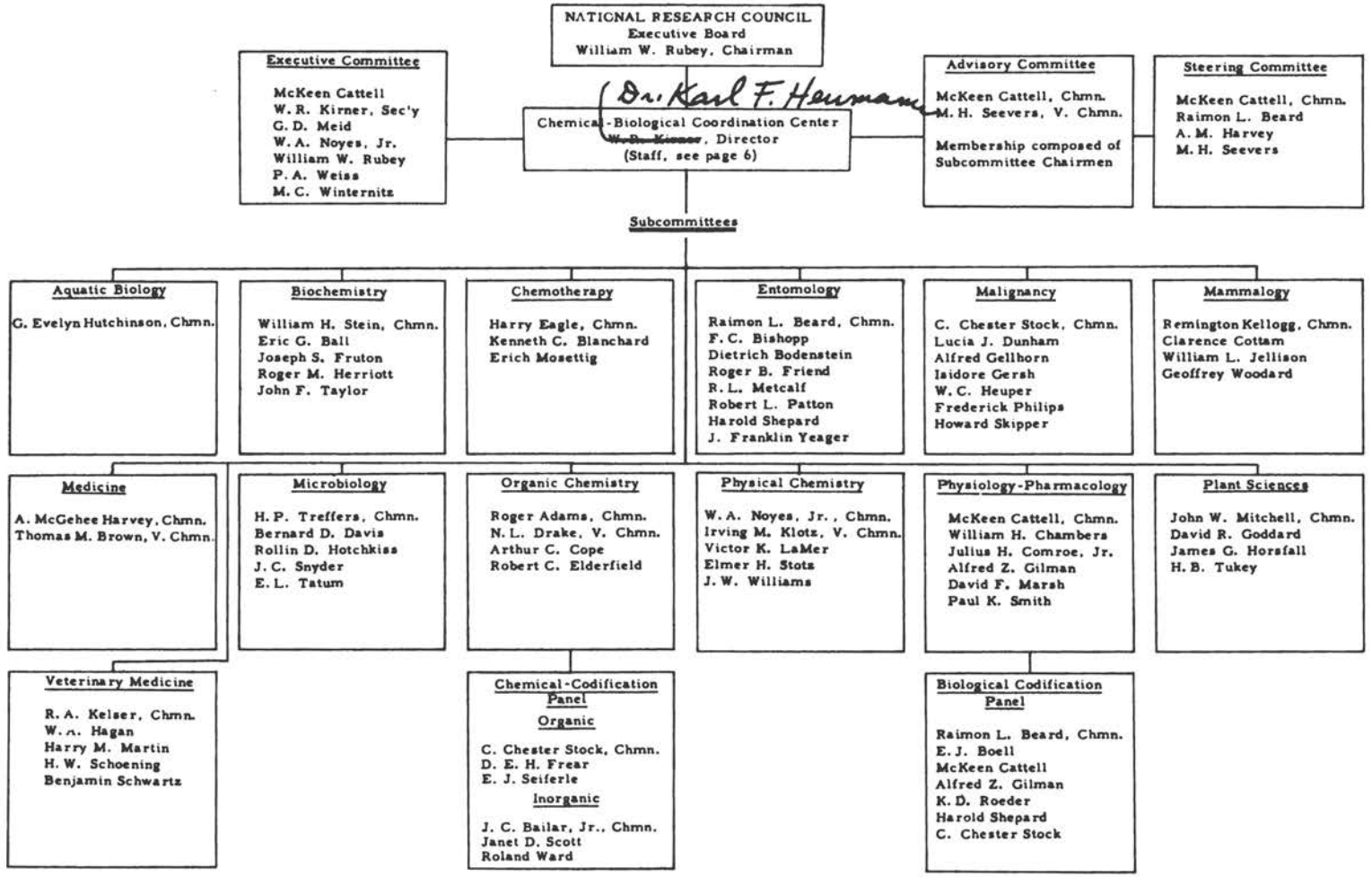
As a result of the above work a considerable amount of information was assembled by the Coordination Center of the Insect Control Committee which concerned the effect of the structure of chemicals upon their insecticidal and rodenticidal activity and upon insect repellency. From 1942 to 1945 more than 8,000 compounds were tested against a variety of insects at the Orlando, Florida, laboratory of the Department of Agriculture. The Food and Drug Administration determined the acute and chronic mammalian toxicity of many of these compounds as well as their skin irritancy. A search for new insecticides was necessary because supplies of pyrethrin and rotenone were cut off by the war. Insect repellents had to be found in order to protect our troops from insect-borne diseases. Similarly, about 1500 compounds were tested against rats at the Patuxent Laboratory of the Fish and Wildlife Service in a search for new rodenticides to be used as substitutes for red squill, strychnine and thallium which were also cut off from the United States. The above investigations were financed by transfer of funds to the appropriate agency by the OSRD and the data were incorporated into the files of the Coordination Center after consideration by the pertinent subcommittees of the Insect Control Committee.

During the war the OSRD financed much additional work which involved the testing of chemicals for various biological activities. Thus, the Board for the Coordination of Malarial Studies sponsored the testing of over 15,000 chemicals for their anti-malarial activity. This work has been summarized in the "Survey of Antimalarial Drugs" edited by Dr. F.Y. Wiselogle. It was necessitated by the fact that the Japanese had gained control of more than 95 per cent of the world's supply of quinine and a substitute had to be found. Division 9 of the National Defense Research Committee prepared and tested nearly 2,000 compounds as candidate chemical warfare agents. The Tropical Deterioration Center sponsored the testing of a large number of compounds to control the action of bacteria, molds and fungi which destroy fabrics, glass, leather, etc. The Chemotherapy Center for Tropical Diseases sponsored the testing of about 1500 compounds against organisms which are involved in schistosomiasis, filariasis, amoebiasis, etc. A number of the Armed Forces technical service laboratories also conducted independent searches for compounds possessing other special biological activities, e.g. the Chemical Warfare Service tested about 2,000 compounds for their action as plant-growth regulators.

Dr. Winternitz, chairman of the OSRD Insect Control Committee, conceived the idea of establishing a Center which would not limit its efforts to the assembly and organization of data concerned only with insect and rodent control problems but rather to extend its scope to include data involving the broad relationships of chemical structure to biological actions of all kinds. All of the above mentioned data would be organized according to a system which would enable them to become readily accessible. In addition, the published literature would be searched for articles which describe the effect of chemicals on biological systems and these data would be organized for use when required. It was also decided to sponsor a screening program which would permit many chemicals to be tested for various biological actions.

Practical uses for otherwise untested chemicals might be found and, at the same time, information would be continuously accumulating concerning the relationship between structure and biological action.

With this broadened objective the Chemical-Biological Coordination Center of the National Research Council was established on July 1, 1946. Subsidy for its support was first provided by the Chemical Corps, the Corps of Engineers, the Air Surgeon's Office, the Surgeon General's Office and the Quartermaster Corps of the Army and the Medical Sciences Division of the Office of Naval Research. Additional subsidy was later provided by the American Cancer Society through the Committee on Growth of the National Research Council, by the National Cancer Institute of the U. S. Public Health Service, by the Bureau of Medicine and Surgery of the Navy and by the Atomic Energy Commission.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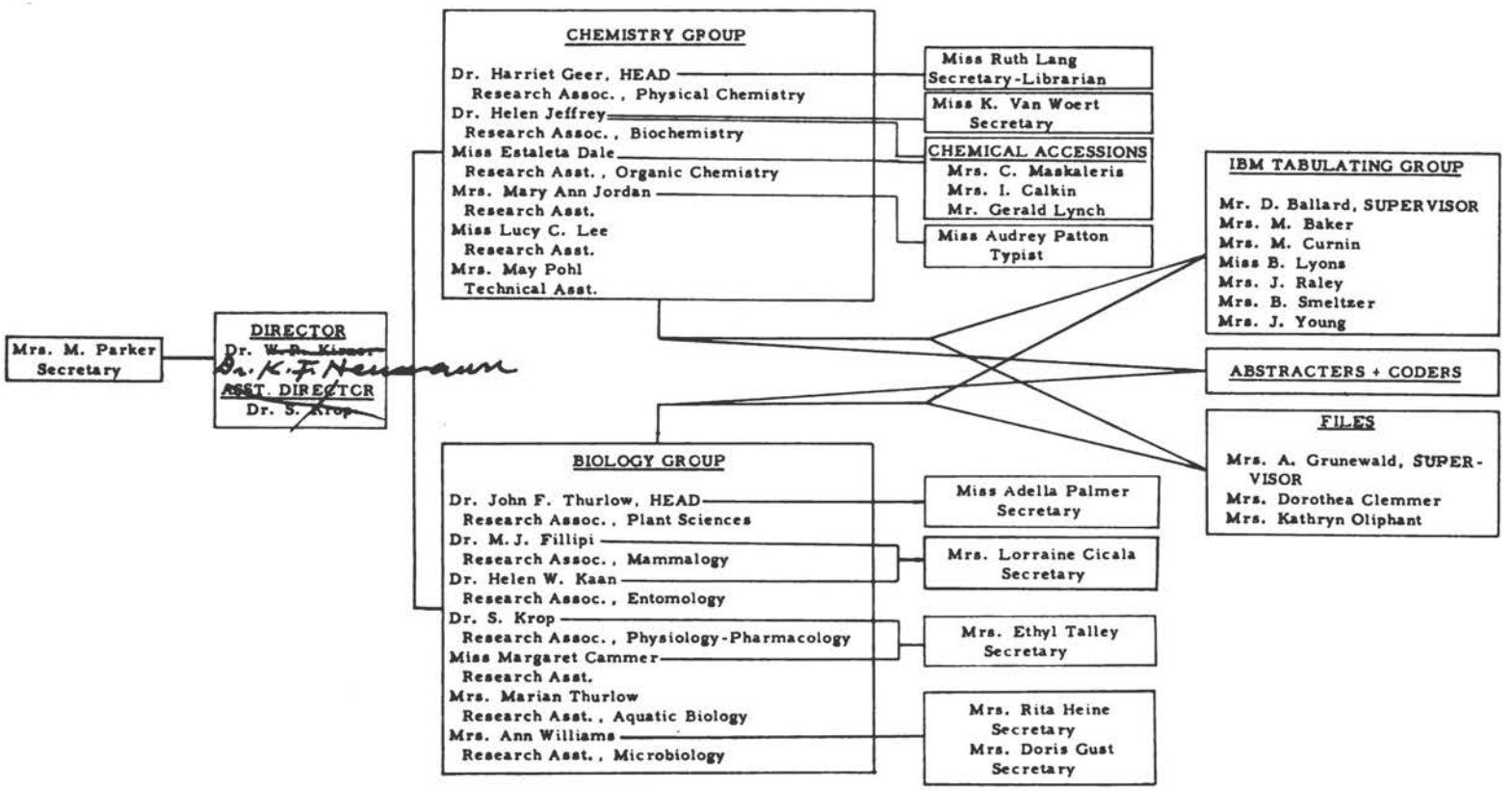


OBJECTIVES

The objectives of the Center are:

1. To assemble and organize information which describes (a) the effect of chemicals on biological systems (plants and animals, their organs, tissues, cells and cell constituents); (b) the metabolism of test chemicals within biological systems; (c) the mechanism of drug action, or provides information leading to an understanding of such action. (See pages 7-19 for details.)

2. To sponsor the preliminary testing ("screening") of compounds on a variety of plants, animals and microorganisms to determine the biological effects of the compounds and to make the resulting data available. (See pages 19-22 for details.)

3. To prepare reviews of the literature on (a) the effect of chemical structure upon various biological actions; (b) test methods used in determining such actions. (See page 23 for details.)

4. To sponsor symposia concerned with the correlation of chemical structure with biological activity. (See page 24 for details.)

THE ASSEMBLY AND ORGANIZATION OF CHEMICAL-BIOLOGICAL DATA

Data Sheets: Chemistry Card Files

Information concerning each individual chemical is recorded on a separate sheet designated as a data sheet. One such sheet is prepared for each chemical which appears in an article, screening report, government publication, etc., which is abstracted by the Center. On one side of this sheet (chemistry side) is recorded the chemical information, e.g., structure, empirical formula, physical state, melting point, boiling point, refractive index, specific gravity, optical rotation, solubility, analytical data, possible impurities, sources, etc. On the other side of the sheet (biology side) is recorded biological information obtained in testing the compound, e.g. test organism used, organ and/or enzyme system involved, dose and/or concentration of the chemical, route and frequency of administration, time of evaluation, biological action, etc. It is therefore possible to obtain with very little difficulty the Center's available information, both biological and chemical, on any compound.

Each chemical is assigned a unique serial number which is recorded on the data sheet. The serial numbers are assigned on the basis of the elements present in the compound. Blocks of numbers are reserved (1) for compounds which contain only carbon and hydrogen; carbon, hydrogen and halogen; carbon, hydrogen and sulfur, etc., (2) for compounds containing only carbon, hydrogen and oxygen, (3) for compounds containing only carbon, hydrogen, nitrogen and oxygen, etc. Thus, in selecting a group of hydrocarbons from the files it is only necessary to consider the block of serial numbers which concern this group and not the entire file. Salts and solvates are assigned the same serial number as the parent compound plus two additional digits. Compounds

containing an abnormal concentration of isotopes are also assigned the same serial number as the parent compound plus two additional letters.

The data sheets are filed according to the above mentioned serial numbers. For each chemical in the data sheet file a chemistry sheet is prepared which precedes the data sheets and summarizes the chemical and physical information contained on the individual data sheets for that chemical.

Although the method of recording chemical information has undergone little change since the Center was organized, a major change in the method of recording biological information was inaugurated in 1951. Previously an abstract or summary of the entire article was prepared for each article assigned to an abstracter. If an article contained chemical-biological information on 50 compounds, 50 copies of this abstract were prepared and the detailed biological and chemical data on each compound were listed against this background. Coders subsequently transferred these data to code sheets from which International Business Machine (IBM) punched cards were prepared. Under the new system, biological summaries or abstracts of this type are not prepared. Instead, all codable biological information on a compound is recorded in the terms of the Detailed Biological Code on the biology side of the sheet. Inasmuch as code symbols are also entered on the biology side at the same time, the information is prepared for punching in a single operation as compared to the previous two-step operation. An important advantage of the recently adopted system is that it permits the checking of the abstracting and coding. Information recorded on both types of sheet is now on file at the Center. The abstract type of data sheet is readily usable by outside investigators whereas the new coded-data sheet, though generally much more efficient, is not readily usable without some instruction by the staff.

The chemical-biological information which is recorded on the data sheets comes from the following sources:

a. Data resulting from the screening program sponsored by the Center.

b. Unpublished data, positive and negative, which are solicited from governmental, industrial and university laboratories.

c. Data from selected scientific periodicals and other published reports.

From a survey of chemical-biological literature, conducted by the staff of the Center, it has been found that it will be necessary to scrutinize approximately 250 selected periodicals (not including those published in Slavic languages) in order to record about 90 per cent of the "useful" data pertinent to the Center's objectives. The Center is at present coding these data from about 45 selected periodicals covering the period from January, 1946, to date. Assignment of the remaining journals to qualified abstracter-coders will be made as funds become available and ultimately the desired data, recorded in all of these journals prior to 1946, will be abstracted. It will be noted that the term "abstracted" is loosely used inasmuch as the procedure now more closely resembles a combined operation of abstracting and coding.

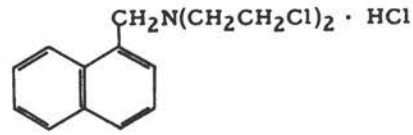
At the present time the Center has about 75,000 data sheets in its files containing chemical-biological information on about 33,000 chemicals. The data sheets filed under a given chemical are numbered serially, in addition to containing the unique serial number mentioned above. The unique serial number is punched on the chemistry punched cards and both numbers just mentioned are punched on the biology punched cards so that after segregating a series of biology punched cards it is possible to make direct reference to the specific data sheets from which the punched cards were prepared. By the use of these numbers it is possible (in the case of the coded-data sheets) to reassemble all the information in any article in the event that such a

procedure is necessary.

The Center also maintains three chemistry card files. One of these has the chemicals filed by serial number, the second by empirical formula and the third by Chemical Abstracts' name. Through the use of the latter two files it is possible to locate the data sheets on any compound even though the unique serial number assigned by the Center is not known. A typical chemistry card is illustrated below.

CBC No. 800,619-10 $C_{15}H_{17}Cl_2N \cdot HCl$

1-Naphthalenemethylamine, N,N-bis(2-chloroethyl)-, hydrochloride



Chemistry Card

The Chemical Code

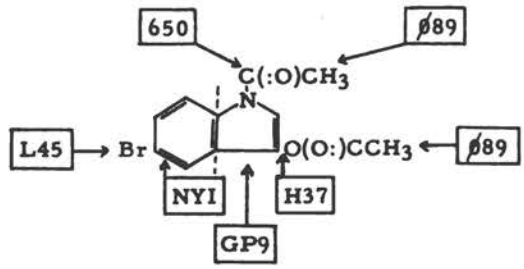
In the spring of 1945, Dr. C. Chester Stock, Executive Secretary of the OSRD Insect Control Committee, was requested by the Committee to investigate the various systems which had been devised for the classification of chemicals in order to determine the possibility of their adaptation for use as a notational system which would facilitate the correlation of chemical structure with biological activity. He soon discovered that Dr. D. E. H. Frear and his associates at the Pennsylvania State College had devised such a system in 1942 and had used it on keysort cards for correlating the structure of several thousand chemicals with their insecticidal and fungicidal activity. The general principles of the Frear system served as a basis for the development of the organic chemical section of the present National Research Council (NRC) Chemical Code. The various necessary modifications and extensions to the Frear system, to adapt it for use with punched cards handled by machines, were made by the Chemical Codification Subcommittee of the Insect Control Committee from the fall of 1945 to July, 1946. Since then the work has been carried on by the Chemical Codification Panel of the Chemical-Biological Coordination Center. The same individuals served on both groups under the chairmanship of Dr. Stock. In the summer of 1946 an Inorganic Chemistry Panel was appointed under the chairmanship of Dr. John C. Bailar, Jr., to extend the NRC Chemical Code to include inorganic chemicals.

The primary purpose in developing the NRC Chemical Code was to arrive at a method of representing chemical structures by linear symbols which could be transferred to punched cards, thus allowing the use of machine methods to assist in the correlation of chemical structure with biological activty. Representation of the component parts

of a compound without showing their connections with one another was considered sufficiently definitive for such purposes. As a result, the code for each compound is not unique and it is seldom possible to reconstruct the complete structure of a compound from the code symbols.

The NRC Chemical Code, entitled "A Method of Coding Chemicals for Correlation and Classification", includes detailed directions for use of the code as well as a list of coded examples. To illustrate briefly the coding of compounds and the information which the code gives concerning the structure of the coded compound, two examples are given below:

Example 1



1-Acetyl-5-bromoindoxyl, acetate

Coded as: 650.1-GP9.1-H37.1-L45.1-NYI.1-ø89.2 (ø = the letter O)

(650 = HC(:O)N-R, H may be replaced by an R group; GP9 = C_4N ring with maximum unsaturation; H37 = RC(:O)OR', R is alicyclic or aliphatic, R' is heterocyclic; L45 = RBr, R is aromatic carbocyclic; NYI = benzene ring fused to a heterocyclic structure; ø89 = C_2 saturated)

Example 2

$K_2Cr_2O_7$

Potassium dichromate

Coded as: RDø.1-T72.2-U63.7

(RDø = K^{+1}; T72 = Cr^{+6}; U63 = (:O) or (-O-))

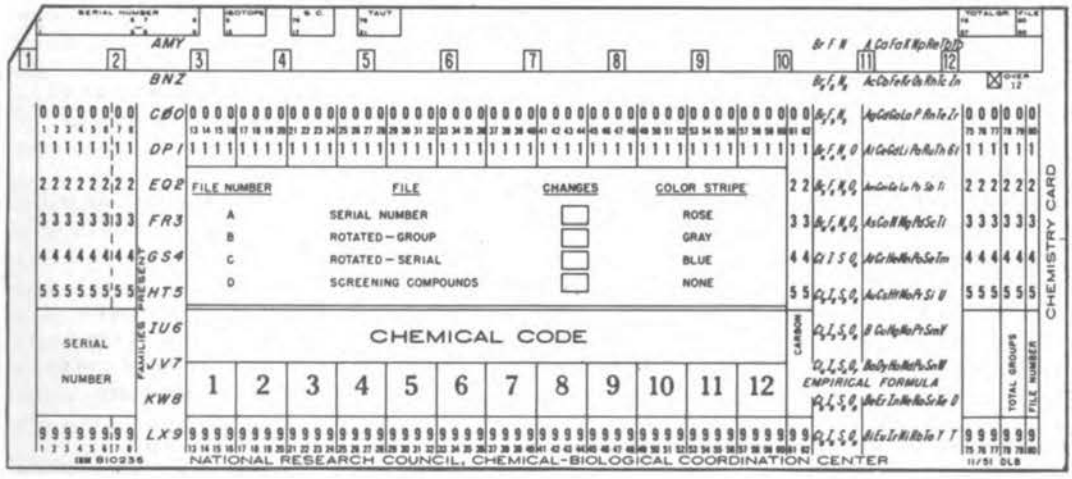
Each code designation contains four numbers and/or letters: the first three describe the component group and the fourth the actual number of times that group occurs in the compound or ion. The code designations are listed in order of the first digit or letter, which is called the family designation. These divide the groups into broad categories. For example, Family 6-- denotes noncyclic groups containing the elements C, N and O; Family G-- ring structures containing C and N; and Family H-- noncyclic groups containing C and O.

In Example 1 above, the code shows the presence of the following groups: a benzene ring fused to a heterocyclic structure (NYI.1), a pyrrole ring (GP9.1), a heterocyclic ester of an alicyclic or aliphatic acid (H37.1), a tertiary amide with the nitrogen as

part of a cyclic structure (650. 1), a bromine attached to an aromatic carbocyclic ring (L45. 1), and two saturated C_2 chains (Ø89. 2). In attempting to reconstruct the structure of the compound from its code, since a single heterocyclic structure containing a single nitrogen fused to a benzene ring is present, it can be concluded that it is an indole or isoindole compound with an acyl group attached to the nitrogen. An esterified hydroxyl group is present on the heterocyclic portion of the fused ring system and a bromine is attached to the carbocyclic portion. Since the only groups unaccounted for are two C_2 chains, a $CH_3C(:O)$- group must be on the nitrogen, and the ester must be an ester of acetic acid. If there had been more than one heterocyclic ring or other additional groups, it would not have been possible to reconstruct the structure of the compound in as great detail.

In Example 2, the presence of K^{+1} (RDØ. 1) and $Cr_2O_7^{-2}$ (T72. 2-U63. 7) is indicated. Family T-- shows that Cr^{+6} (-72) is the central element of an anion. R72 would have indicated Cr^{+6} (-72) as the central element of a cation or neutral molecule. Family U-- shows seven oxygen atoms coordinated to an element coded in Family T--.

The chemistry punched card is illustrated below:



Chemistry Punched Card

It may be noted that space for twelve code designations has been allotted on the chemistry punched card. When more than twelve different groups are present, this is indicated by a supplementary punch and the remainder of the chemical code is placed on a second card. As aids in sorting, the families present corresponding to the first symbol of the code designations and the empirical formula are included on the punched card. This is not a true empirical formula since the actual number of atoms present is shown only for C, Br, Cl, F, I, N, O and S, whereas for other elements only their presence is indicated. Specific punches are also used to indicate the presence of a radioactive element and/or an abnormal concentration of isotope.

In 1948, a trial of the chemical code was conducted with about 3,000 compounds. At that time certain changes were made in the code as a result of its use in answering questions by machine methods. Approximately 33,000 compounds from the Center's

files have now been coded using the present NRC Chemical Code.

Copies of the code are now available at $1.50, postpaid. Those interested in acquiring a copy should direct their requests to the Publications Office, National Academy of Sciences, 2101 Constitution Avenue, N. W., Washington 25, D. C.

Biological Codes

In April, 1946, the Biological Codification Committee of the OSRD Insect Control Committee was organized with Dr. McKeen Cattell as chairman. This Committee, which later became the Biological Codification Panel of the Chemical-Biological Coordination Center, was called upon to formulate a system for classifying and codifying fundamental biological activities of chemical compounds in such a way as to permit the transfer of these data to punched cards which could then be manipulated mechanically by means of IBM equipment. The objective was to make possible the rapid assembly of information on chemicals with reference to a variety of aspects of their chemical structure, physical properties and biological actions. The scope of the actions to be catalogued included physiology, pharmacology, toxicology and enzymology, considering all organisms. To facilitate the work of the Panel, the various subcommittees of the Center were asked to cooperate by providing information which they felt was necessary for the expression of biological actions in their respective fields.

The problem was one of cataloguing biological actions in such an inclusive way as to cover all the desired information and yet be exclusive enough to serve in indicating correlations, particularly those relating to chemical structure and biological response. The adaptation of the system to punched cards imposed some limitations, but the program has been pursued on the premise that only by the use of mechanical aids will it be possible to handle efficiently the mass of information which ultimately will be in the files of the Center.

The development of such a classification has not been easy. Because no previous system applicable to the machines and all fields of biology was available to serve as a model, the Panel proceeded in an experimental manner. As a result, several codes have been developed and tested at the Center for their application to the problem.

Early in the program it seemed desirable to devise a general biological code to describe the broad fundamental actions of many compounds and to answer the question: "What biological tests have been performed with a given type of chemical?" The need for a code was emphasized by the accumulation of data resulting from the war-stimulated screening programs particularly for antimalarials, insecticides, rodenticides, fungicides and plant growth regulators. The General Biological Code was thus developed to meet the practical needs of the moment. This code was designed to occupy the space on a punched card not occupied by the chemical code and was to be used in conjunction with it. This space amounted to 23 columns each of which contained 12 punching positions, or a total of 276. The General Biological Code was based on the principle of direct coding, in which each punch designated a single unique concept which was independent of all other concepts. Thus there was opportunity for expressing 276 different ideas. Of these, 211 were utilized, representing subdivisions of the following major considerations:

Taxonomic groups of microorganisms and plants
Physiological actions of plants
Taxonomic groups of invertebrates
Physiological actions of invertebrates
Population control of microorganisms
Population control of invertebrates

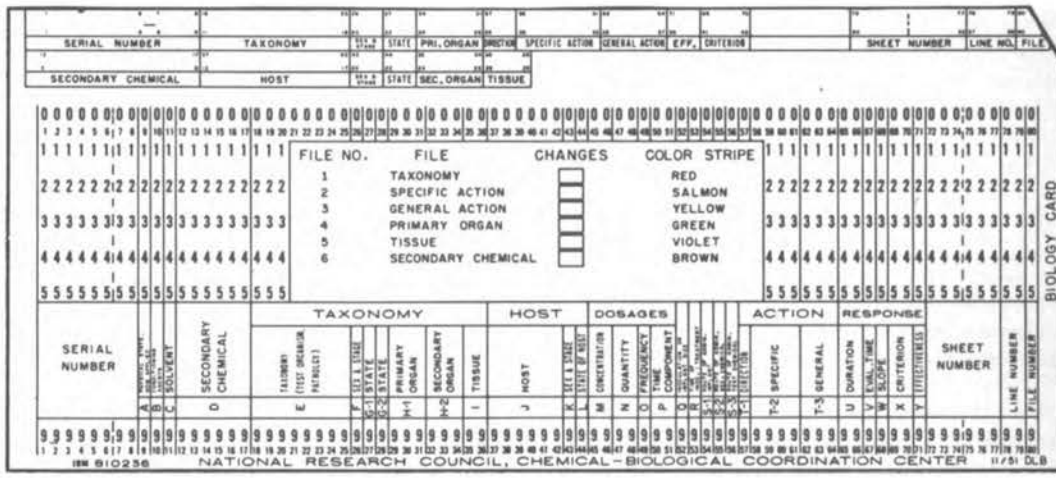
Chemotherapeutic action against parasitic infections
Enzymes
Carcinogenic and carcinoclastic action
General physiological actions pertaining to
microorganisms, plants and animals
Taxonomic groups of vertebrates
Morphology and pharmacology of vertebrates

In using the General Biological Code on punched cards, all of the biological information classified according to the code was indicated on the one card together with the chemical information. This code provided for recording positive or negative biological activity, but the degree of activity was not expressed.

The usefulness of this code was largely limited to providing a general summary of the actions of a compound and to designating the fields of study to which the compound had been subjected. Many desired correlations could not be made because of the lack of specificity in many of the categories and because the degree of activity was not indicated. Moreover, the application of direct coding introduced difficulties in machine operation which required special handling in entering new information, in maintaining useful files and in seeking answers to questions put to the system. For these and other reasons the General Biological Code was felt to be unsatisfactory for the long-term objectives of the Center and is no longer in use.

The Biological Codification Panel, which has been under the chairmanship of Dr. Raimon L. Beard since July, 1950, undertook the development of detailed codes when the limitations of the General Biological Code were confirmed. Dr. Beard spent a month at the Center in the spring of 1950 working with the staff. During this time the basic development of the detailed codes was completed. Further developments involved the assistance of the Biological Codification Panel, the Center's subcommittees and staff. While the development of the Detailed Biological Code has been a cooperative venture, Dr. Beard has contributed most to bringing it to its present state of completion. These codes, now incorporated into a single Detailed Biological Code, will permit more specific answers to questions on biological actions. Furthermore, more extensive correlations can be made and the problems of maintaining the file of punched cards are considerably reduced.

The Detailed Biological Code is designed to be of sufficient detail to permit correlations, particularly those relating to chemical structure and biological response, but not so detailed that each bit of information becomes unique. It is an indexing system permitting a multiplicity of cross referencing which makes possible the selection of many different combinations of ideas. In using the Detailed Biological Code each observation is placed on a separate punched card. The biology punched card, illustrated below, is divided into fields as follows:



Biology Punched Card

IBM Card Column No.	Field	Description of Information Coded in Each Field
1-8	-	Compound serial number
9	A	Physical state of compound; how applied
10	B	Conditioning agent
11	C	Solvent
12-17	D	Serial number of compound against which the test compound is compared; is a synergist; is an antagonist, etc.
18-25	E	Test organism; tumor; pathological condition
26	F	Sex and stage of development of test organism
27	G-1	State of organism or organ
28	G-2	Second state of organism or organ
29-31	H-1	Primary organ system
32-34	H-2	Secondary organ system
35-36	I	Tissues, cells, fluids
37-42	J	Host organism; test environment
43	K	Sex and stage of development of host
44	L	State of host organism or organ
45-46	M	Dosage - concentration
47-48	N	Dosage - quantity
49	O	Dosage - frequency
50-51	P	Dosage - duration
52	Q	Size of inoculum
53	R	Time of treatment relative to time of inoculation
54	S-1	Route of administration, inoculum
55	S-2	Route of administration, compound expressed in D
56	S-3	Route of administration, test compound
57	T-1	Action - direction of
58-61	T-2	Action - specific
62-64	T-3	Action - general
65-66	U	Action - duration of; persistence of residue
67	V	Evaluation time
68	W	Slope of dosage response curve
69-70	X	Criterion of response

IBM Card Column No.	Field	Description of Information Coded in Each Field
71	Y	Summary of effectiveness
72-77	-	Serial number of data sheet
78-79	-	Area of data sheet from which the coded information was taken (code line number)
80	-	Reserved for use of tabulating department

It can be seen that it is possible to code a description of an observation on the effect of a compound on a biological system with details of the system affected, technique of application and type and degree of response. The code, then, provides for expressing an experimental result in sentence form, saying, in effect, that a certain compound, under the conditions stated, is effective to the degree stated in producing a certain action in certain structures of a specified organism. The following example illustrates the manner in which a single observation is coded. Code symbols are not indicated but the fields in which the data are coded are designated.

Example: "Parathion" was added to an aqueous solution (to obtain a concentration of 1×10^{-6}M) containing cholinesterase obtained by preparing a brei of the brains of adult female bees. Inhibition was found to be 50% after 10 minutes of elapsed time.

In terms of the code this observation would produce a single line of code (one punched card) which would read:

Test Compound	A	C	E	F	G-1	H-1	M
Parathion	in solution	water as solvent	bee as test organism	adult females	brei of	brains	test compound in concentration of 1×10^{-6}M

O	P	S-3	T-1	T-2	V	X	Y
applied continuously	for ten minutes	in a bath containing the brains	inhibits	action of cholinesterase	observed after ten minutes	by code scale No. 51	is found to be highly effective

It will be noted that the data undergo a certain amount of translation in order to be coded, e.g. 50% inhibition is not coded as such but this figure is used in ascertaining the relative effectiveness of the compound based on one of the standard scales of effectiveness in the code. The above example does not illustrate the uses of all fields but does provide some understanding of the basic principles which are followed.

During the early part of 1951 the Center, in collaboration with its subcommittees and the Biological Codification Panel, undertook an extensive test of the Detailed Biological Code. More than fifty questions from such diverse fields as pharmacology, entomology, plant pathology, plant physiology and bacteriology were used to test the adequacy of the code and the techniques which are involved in the use of the IBM machines and punched cards. The test served to detect certain weaknesses, which have been corrected, and to demonstrate the general workability of the code in all branches of science to which it has been applied. It was found that the most serious

limitation on providing meaningful answers to questions was the lack of coded data. This discovery was not unexpected. It takes time to assemble and organize the mass of data which fall within the scope of the Center's interests. As the Center continues to accumulate punched cards in additional fields of science the problem of inadequate data will gradually be solved. Until this matter is entirely overcome, however, the Center will be able to provide much more complete information in certain areas where much coding has already been done, e.g. entomology, whereas in other areas only partial answers can be supplied.

Use of Punched Cards

Since the data sheets are filed in serial number order, it is apparent that some efficient index is needed to the chemical and biological information which they contain. As a facility in searching for such information the Center uses punched cards and standard IBM machines, namely, punches, sorters, an interpreter, a reproducer, a collator and an alphabetic tabulator. All operations are, at present, conducted by a group of six machine operators and a supervisor.

All of the chemistry punched cards contain the serial number, families present, chemical code and elements present as shown on page 11. Two separate files are maintained, one in serial number sequence and the other in sequence of the code designations. The latter file, called the "rotated" file, requires the preparation of as many cards as there are code designations. The rotation is accomplished by shifting the code designations in the first field to the second field, the second to the third, etc., and from the last field back to the first field. Consequently, each code designation appears in turn in the first field on the left-hand side of the card. This field is used as the filing sequence for the "rotated" file. For example, three cards are prepared for a compound coded as A42.1-NYR.1-Ø99.1 with the following sequence of the code designations: (card 1) A42.1-NYR.1-Ø99.1, (card 2) Ø99.1-A42.1-NYR.1 and (card 3) NYR.1-Ø99.1-A42.1. The entire "rotation" operation is accomplished automatically on the reproducing punch.

The biology punched cards contain all the coded biological data for each test performed. Replicates of these cards are filed in code number sequence under each of the following major coding fields:

(a) Test Organism
(b) Specific Action
(c) General Action
(d) Tissue
(e) Organ
(f) Secondary Chemical

In addition to the above files a cumulative file of all cards for each compound is maintained in serial number sequence.

Some of the typical operations performed upon the punched cards by the machines will be explained at this point. The relationship of the operations in the ultimate answering of questions will be shown later. (See pages 17-19 for details.)

Sorting has two general applications. The first and more obvious is that of arranging a file of punched cards in a given sequence, for example, in ascending serial number order. The second is in selecting a given card or a related group of cards, from a file not already in such order, so that rapid hand selection of the desired items can be made.

Collation has a wide range of applications but those most important to the Center are: (1) checking the filing sequence in files; (2) merging two or more separate groups of cards into one combined file; (3) matching two or more groups of cards for some coincidence of a desired characteristic and (4) the selection of some desired combination of information on certain cards without disturbing the original order of the remaining card file. The matching operation is probably most useful in answering questions. The files are maintained in various orders for rapid hand selection of each component of the answer. These files are also arranged in serial number order within each major division and permit direct comparison by the collator of corresponding serial numbers within the several files. By this procedure it is possible to determine which compounds possess, simultaneously, the desired characteristics.

Automatic reproduction of all or any part of the card may be accomplished on the reproducing punch. This, of course, permits establishing, at will, new or specialized files from existing cards. The same machine is also used to verify the accuracy of the original transcription of data to the cards by comparing the punches in two sets of cards each punched by different punch operators.

The alphabetic tabulator furnishes the medium for producing printed lists of serial numbers, data sheets, codes, etc., from the cards which have been selected in answer to any given question. It is also used to print lists of test organisms and their code numbers for use by the coders. The use of the punched cards for this purpose obviates the need for proofreading manually prepared lists.

Records are maintained on the number of punched cards filed under each code designation so as to expedite the selection of the most efficient searching procedure to use in answering a given question.

USE OF THE CENTER'S FILES FOR ANSWERING QUESTIONS

The data in the files of the Center are available to representatives of its sponsoring agencies, screening agencies and to authorized scientists, upon request. The following examples illustrate the use of the chemistry card files, the data sheet files and the punched card files in answering questions. Simple examples have been selected to illustrate the operations which lead to the answer; similar procedures are used in answering more complex questions. It should be emphasized that there is no fixed procedure in the mechanics of answering a given question because the answer may be approached in one of a number of ways. Sometimes the approach is from the chemical side and sometimes from the biological side. The result obtained in a given step in a procedure often determines the nature of the succeeding step.

Chemical-Biological Correlation Questions

(a) What information is available on a specific biological action of a single compound? e. g. "Does trasentin have local anesthetic activity?" To answer this question the serial number of trasentin is located in the chemistry card file. The data sheets bearing this number are inspected and if relatively few in number they are scanned. If many data sheets are present all punched cards bearing this serial number are selected, either manually or by machine, from among those in the biological action punched card files in question, viz., "local anesthetic" (General Action File) and "conduction block" (Specific Action File).

(b) What information is available on the biological actions of a single compound? e. g. "What are the biological actions of, or what biological tests have been performed with 2,6-diaminopyridine?" To answer this question the serial number of the compound is first determined. Then a listing of data sheets is made from the cumulative punched card file which is maintained in serial number order. The selected data sheets are examined for the biological actions which they describe.

(c) What information is available on a specific biological action of a series of compounds of similar structure? e. g. "What derivatives of ethylenediamine have antispasmodic activity?" Definition of the term "derivatives" is required before answering the question; if, for example, tertiary diamines having at least one alkyl group on each nitrogen atom were the derivatives in question, the chemical code designations for such compounds would be F51 (R-NR'), F54 (R, R', R"N where R, R', R" are alicyclic or aliphatic), F56 (where R, R', R" are heterocyclic and alicyclic or aliphatic), and F57 (where R, R', R" are aromatic carbocyclic and alicyclic or aliphatic). The punched cards bearing such code designations are hand-selected from the rotated chemistry punched card files and machine-sorted in the empirical formula columns for cards limited to compounds with two or more nitrogen atoms. Such cards are collated with all punched cards containing data on antispasmodic activity (biology punched cards bearing the code number for "antispasmodic" in the General Action File and Muscle Contraction in the Specific Action File), rejecting all cards on compounds tested for antispasmodic activity but found ineffective. The remaining cards are checked with the chemistry card file (serial number file), eliminating the cards representing compounds which are not derivatives of ethylenediamine.

(d) What information is available on the biological actions of a series of compounds of similar structure? e. g. "What are the biological actions of compounds containing a benzene ring with one or more chlorine atoms attached and having an LD_{50} of >50 mg/kg for mammals and an LD_{50} of <5 mg/kg for insects?" To answer this question, the punched cards filed under "acute toxicity" and "chronic toxicity" in the Specific Action File are machine-sorted for all cards dealing with insects and combined with those under Insecticide in the General Action File; from the resulting cards those indicating inactivity are eliminated and the remainder sorted for those showing a dosage of < 5 mg/kg in Field N and dose-response in Fields X and Y. The process is repeated for mammals. The cards resulting from the two operations are collated with cards from the rotated chemistry punched card file representing compounds containing chlorine attached to an aromatic carbocyclic ring. The resulting cards are checked visually with the chemistry card file for the occurrence of a benzene ring with chlorine(s) attached. The cards so segregated yield the serial numbers of the compounds sought; the final operation involves, after eliminating those concerning "acute toxicity" and "chronic toxicity" (since these are not needed for the answer), listing of data sheet numbers of the compounds. The data sheets are examined for biological actions.

Many questions concerning structure/activity are encountered which, at first glance, seem to be quite different from the above four illustrations. However, closer inspection will disclose that they fall into one of the above four categories. Thus, the questions "What carcinogenic compounds contain the dibenz[a, h]anthracene ring system?" and "What toxicity data are available on a simple Mannich base such as $CH_3COCH_2CH_2N(CH_3)_2$ and its higher homologs?" are variants of question (c). Questions such as "Have any beta substituted glutaric acid imides been tested for biological activity?" and "What compounds have been found to have local anesthetic but not skin irritating activity in rabbits?" are variations of question (d).

It is the ultimate purpose of the files to facilitate correlation i. e. deduction of generalizations governing the relationship between chemical structure and biological activity. After a deck of biology punched cards has been segregated in answering a

question and grouped according to activity, the frequency of occurrence of certain chemical groupings in each category can be tabulated from the rotated chemistry punched cards. Plotting frequency against activity may allow inferences to be drawn concerning the probabilities of enhancement or suppression of action by a given substituent. The files may also be used to confirm generalizations after they have been deduced as well as to determine exceptions or substantiate suspected correlations which could prove helpful in a search for more potent compounds.

Chemical Questions

In assembling and organizing chemical-biological data, the Center records the sources of supply of many chemicals of interest to investigators. A knowledge of the possible sources of such chemicals can prove extremely useful. Consequently the Center will attempt to provide answers to questions such as:

(a) What is the source of a certain chemical? e. g. "What is a possible source of supply of homolysine?" This question would be answered by consulting the data sheets filed under the serial number of homolysine, the various commercial catalogues on file, and/or Chemical Abstracts. The use of the punched card file is not necessary in answering this type of question.

(b) From whom can a given series of compounds of defined structure be obtained? e. g. "What thiosemicarbazones are included in the Center's files and what are their possible sources?" This question would be answered by a combined use of the chemistry punched cards, the screening program files and the data sheet file. The chemical code designation covering thiosemicarbazones is 820. The punched cards bearing this code designation would be selected from the rotated, chemistry punched card file and their serial numbers listed on the tabulator. The sources of the screening compounds would be found in the screening program files and the sources of the remaining compounds would be sought in the data sheet file.

THE SCREENING PROGRAM

The Screening Program sponsored by the Center has as its objective the broad preliminary testing of chemicals for their biological effects on a variety of microorganisms, plants and animals. This testing is done in an endeavor to find uses for those chemicals which have not been previously tested or which have been subjected to a limited number of tests. The laboratories, designated as screening agencies, which conduct the screening tests are all associated with non-profit institutions and are officially approved by the Center's Advisory Committee on the recommendation of the appropriate subcommittee (see page 5). After being approved each screening agency is required to sign a statement in which it is agreed that the agency will provide the Center with a complete description of the techniques used in conducting tests on the compounds provided by the Center and will report all test data, whether positive or negative, including a statement concerning any compounds which could not be tested because of insolubility, volatility, etc.

Chemicals for the screening program are solicited from university, governmental and industrial laboratories. Upon offering compounds to the Center for screening, the submitters are provided with forms on which to record the chemical and physical properties, any known biological effects of the compounds, and the amounts available

for distribution. This information is then circulated in the form of accession lists, (one hundred compounds per month) to the screening agencies which select the compounds they would like to test, indicating the minimum quantity of each compound needed. These summarized requests are, in turn, forwarded to the submitters and the compounds are distributed to the screening agencies as soon as they are received by the Center. Compounds made available on accession lists are sent to the screeners usually within three months from the time they are selected. The quantity of a compound offered by the submitter is often inadequate to meet all requests, and in these cases the distribution is decided by a priority committee.

Results of the tests performed by the screening agencies are reported to the Center within a specific time limit which depends upon the time required for a given test. The maximum time requirement for the majority of tests can be approximated as six months. These results are promptly reported to the submitter of the compounds concerned after they are received by the Center. Following this and after a suitable time lapse, established as three months, these data are incorporated into the Center's files and are available to authorized investigators. If a compound appears to be of specific interest after preliminary tests the Center assists in establishing contact between the submitter and the screening agency. In the event that practical uses are found for the compounds submitted through the Center, the Center will not concern itself with the filing of patent applications.

In conjunction with the official screening program the Physiology-Pharmacology, Microbiology and Biochemistry Subcommittees of the Center sponsor special testing programs in several fields of pharmacology, virus chemotherapy and intermediary metabolism, respectively. This phase of the Center's screening program is an aid to scientists, either submitters or screeners, who desire compounds to be subjected to specific tests outside of the scope of the Center's cooperating screening agencies or who desire to test specific types of compounds for more complete studies of structure-activity relationships. If a submitter should request that compounds be subjected to specific tests for which the Center has pre-arranged facilities, the Center will undertake such testing without entering the compounds on the accession lists. If the desired test is not currently included, the matter is brought to the attention of the appropriate subcommittee of the Center to recommend a laboratory which is prepared to perform these tests. Conversely, if a screening laboratory is desirous of testing certain types of compounds, the Center will make an effort to obtain these compounds.

Data obtained from the screening program may not be published or referred to in articles for publication without the permission of the screening agency concerned. The Center makes these data further available in the Summary Tables of Biological Tests (see page 24). These Tables present the serial number, name, structure and source of the chemicals and, in summarized form, the technique and the results of the tests. Appearance of results in these Tables are contingent upon the statements set forth above.

The screening agencies have been notified of the availability of 4300 compounds in 43 accession lists. Approximately 8500 test data have been reported to the Center from the screening laboratories. Among the reports received several groups of compounds have shown promising results in the initial phase of testing. These compounds are being further investigated for confirmation of their biological activity.

List of Screening Agencies

1. Chester Beatty Research Institute, Royal Cancer Hospital, London, England. Dr. Alexander Haddow (Cancer)

2. Chemical Corps, Biological Laboratories, Camp Detrick, Maryland. (Plant Growth Regulators and Fumigants)

3. Chemical Corps, Medical Laboratories, Army Chemical Center, Maryland. (Toxicity)

4. Connecticut Agricultural Experiment Station, New Haven, Connecticut. Dr. James G. Horsfall (Insecticides and Fungicides)

5. * Georgetown University Medical School, Washington, D.C. Dr. Martin Rubin (Cancer)

6. * Hawaii Marine Laboratory, University of Hawaii, Honolulu. Dr. Robert W. Hiatt (Dispersion of Schools of Fish)

7. Henry Phipps Institute, The University of Pennsylvania, Philadelphia, Pennsylvania. Dr. E. R. Long (Tuberculosis)

8. Iowa State College, Ames, Iowa. Dr. C. H. Richardson (Insecticides)

9. Michigan State College, Lansing, Michigan. Dr. H. B. Tukey (Plant Growth Regulators and Antibacterials)

10. National Research Council, Prevention of Deterioration Center, Washington, D. C. (Fungicides and Bactericides (materiel))

11. Pineapple Research Institute of Hawaii, Honolulu. Dr. Willis A. Gortner (Plant Growth Regulators)

12. Quartermaster Corps, Department of the Army, Washington, D. C. Dr. Ray Treichler (Bactericides and Fungicides (materiel))

13. Rhode Island Agricultural Experiment Station, Kingston, Rhode Island. Dr. Frank L. Howard (Fungicides)

14. Rothamsted Experimental Station, Harpenden, Herts., England. Dr. C. D. Potter (Insecticides)

15. Sloan-Kettering Institute for Cancer Research, New York, New York. Dr. C. Chester Stock (Cancer); Dr. Frederick Philips (Toxicity)

16. Suffield Experimental Station, Suffield, Alberta, Canada. (Insecticides and Fumigants)

17. Trudeau Laboratory, Trudeau, New York. Dr. A. J. Vorwald and Mr. W. Steenken (Tuberculosis)

18. U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine, Anaheim, California. (Insecticides)

19. U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine, Orlando, Florida. (Insecticides and Insect Repellents)

20. U. S. Department of Agriculture, Bureau of Plant Industry, Soils and Agricultural Engineering, Division of Fruit and Vegetable Crops and Diseases, Beltsville, Maryland. (Plant Growth Regulators)

21. U. S. Department of Agriculture, Bureau of Plant Industry, Soils and Agricultural Engineering, Division of ~~Fruit and Vegetable Crops and Diseases~~ Weed Investigations, Beltsville, Maryland. (Herbicides)

22. U. S. Department of Agriculture, Bureau of Plant Industry, Soils and Agricultural Engineering, Division of Fruit and Vegetable Crops and Diseases, Orlando, Florida. (Citrus Fruit Decay Preventatives)

23. U. S. Department of Agriculture, Bureau of Plant Industry, Soils and Agricultural Engineering, Central Florida Experiment Station, Sanford, Florida. (Nematocides)

24. U. S. Department of Interior, Fish and Wildlife Service, Great Lakes Fishery Investigations, Ann Arbor, Michigan. (Sea Lamprey Larvae Toxicity Tests)

25. U. S. Department of Interior, Fish and Wildlife Service, Kearneysville, West Virginia. (Treatment and Prevention of Diseases of Fresh Water Fish)

26. U. S. Department of Interior, Fish and Wildlife Service, Patuxent Economic Investigations Laboratory, Laurel, Maryland. (Rodent Repellents)

27. U. S. Department of Interior, Fish and Wildlife Service, Wildlife Research Laboratory, Denver, Colorado. (Rodenticides)

28. U. S. Naval Medical Research Unit No. 3, Cairo, Egypt. (Molluscicides)

29. U. S. Public Health Service, Communicable Disease Center, Savannah, Georgia. (Insecticides and Rodenticides)

30. U. S. Public Health Service, National Institutes of Health, Bethesda, Maryland. (Cancer, Malaria, Tuberculosis, Tropical Diseases and Other Diseases)

31. University of California Citrus Experiment Station, Riverside, California. Dr. A. M. Boyce (Insecticides)

32. University of California Medical School, Berkeley, California. Dr. David M. Greenberg (Acute Toxicity and Cancer)

33. University of Rochester School of Medicine and Dentistry, Rochester, New York. Dr. Harold C. Hodge (Anti-convulsants and Relaxants)

34. University of Toronto, Connaught Medical Research Laboratories, Toronto, Canada. Dr. C. E. van Rooyen (Viricides)

35. Washington University, St. Louis, Missouri. Dr. Barry Commoner (Inhibition of Plant Viruses)

36. Western Reserve University, Department of Medicine, Cleveland, Ohio. Dr. R. I. Dorfman (Androgens)

* Provisional

PUBLICATIONS

Reviews Concerning Structure-Activity Relationships

At periodic intervals the Center publishes reviews concerned with various structure-activity relationships of chemicals. These publications are designated as CBCG Reviews and are sponsored by the appropriate subcommittee of the Center. To date three such reviews have been published:

CBCC Review No. 1 "The Mode of Action of Organic Insecticides" by Dr. R. L. Metcalf of the University of California Citrus Experiment Station. 84 pp. December 1948. $1.00 postpaid.

CBCC Review No. 2 "Monofluoroacetic Acid and Related Compounds" by Dr. M. B. Chenoweth of the University of Michigan Medical School. 42 pp. January 1950. $0.50 postpaid.

CBCC Review No. 3 "Histamine Antagonists" by Dr. Frederick Leonard of the Warner Institute of Therapeutic Research and Dr. Charles P. Huttrer of the Chemical-Biological Coordination Center. 122 pp. December 1950. $1.50 postpaid.

Two
~~Four~~ reviews are in preparation:

CBCC Review No. 4 "The Bacteriostatic Activity of 3500 Organic Compounds for Mycobacterium tuberculosis var. hominis" by Dr. Guy P. Youmans, Mrs. Anne S. Youmans of Northwestern University Medical School and Mr. Leonard Doub of Parke, Davis and Co. (On press)

CBCC Review No. 5 "Relationship Between Chemical Structure and (1) Rat Toxicity and (2) Rat Repellency" by (1) Dr. James B. DeWitt, Mr. Ervin Bellack, Dr. Clarence W. Klingensmith, Mr. Justus C. Ward and Dr. Ray Treichler and by (2) Mr. Ervin Bellack, Dr. James B. DeWitt and Dr. Ray Treichler of the Patuxent Research Refuge, Fish and Wildlife Service, U.S. Department of the Interior.

CBCC Review No. 6 "The Relationship of the Structure of 8-Aminoquinolines to their Antimalarial Activity" by Dr. L. H. Schmidt, Institute of Medical Research, The Christ Hospital, Cincinnati, Ohio.

CBCC Review No. 7 "Histamine-Histidine" by Dr. Charles P. Huttrer, Division of Research Grants, National Institutes of Health, and Dr. Stephen Krop, Chemical-Biological Coordination Center.

Reviews Concerning Test Methods

"Test Methods in Entomology". The preparation of this book is being sponsored by the Center's Entomology Subcommittee. It will include descriptions of toxicological and screening methods employed by entomologists in the United States and other countries. Dr. Harold H. Shepard, editor.

"Summary Tables of Biological Tests"

These Tables contain data resulting from the screening program sponsored by the Center. They are issued bimonthly.

Volume 1, (2 Nos. only). 120 pp. 1949.

Volume 2, (6 Nos.) 370 pp. 1950.

Volume 3, (6 Nos.) 372 pp. 1951.

An index (chemical names and empirical formulas) has been completed for Volumes 1-2. 116 pp. September 1951. Indexes will be prepared for future volumes as completed.

Subscription Rates (Postpaid):

Volume 1	$1.00
Volume 2 plus index to Vols. 1-2	3.50
Volume 3 plus index	3.50
Volume 4 (1952) plus index	3.50
Indexes (Vols. 1-2, Vol. 3 and Vol. 4)	1.00 each
Single numbers of any volume	0.50 each

Codes

The National Research Council Chemical Code entitled "A Method of Coding Chemicals for Correlation and Classification" was developed by the Center's Chemical Codification Panel. 98 pp. July, 1950. $1.50 postpaid.

The Detailed Biological Code developed by the Center's Biological Codification Panel with the assistance of the various subcommittees and staff of the Center will be published in 1952.

Symposium Volumes

The papers and discussions presented at the Center's first symposium on "Chemical-Biological Correlation", which was held in Washington on May 26-27, 1950, will be published in January, 1952. Now available – $4.00

The Center's second symposium, entitled "Mechanism of Drug Action and Drug Resistance", will be held at the National Academy of Sciences, Washington, D. C., on October 24-25, 1952. The second symposium volume will contain the papers presented at this meeting.

Miscellaneous (Distributed free, upon request, if still available)

1. "Instructions for Using Sodium Fluoroacetate (Compound 1080) as a Rodent Poison". 11 pp. October, 1948. This brochure was prepared by the Center's Mammalogy Subcommittee in cooperation with the Fish and Wildlife Service.

2. "Interim Recommendations for the Treatment of Fluoroacetate Poisoning" was prepared by the Center's Physiology-Pharmacology Subcommittee. 2 pp. April, 1950.

3. "Coding and Sorting Chemical Compounds by Means of Punched Cards" by John A. Morgan and D. E. H. Frear, J. Chem. Education, 24, 58 (1947). (Supply exhausted)

4. "The Use of Punched Card Techniques in the Coding of Inorganic Compounds" by John C. Bailar, Jr., Karl F. Heumann and Edwin J. Seiferle, ibid, 25, 142 (1948).

5. "The Work of the Chemical-Biological Coordination Center in Relation to Chemotherapy in Veterinary Medicine" by Dr. J. R. M. Innes, J. Am. Vet. Med. Assoc., 116, 22 (1950).

6. "The Chemical-Biological Coordination Center of the National Research Council" by Dr. H. W. Kaan, Proceedings of the 8th International Congress of Entomology, pp. 920-3 (1950). (Supply exhausted)

7. "The Chemistry and Physiological Action of Khellin and Related Products" by Dr. Charles P. Huttrer and Miss Estaleta Dale, Chem. Reviews, 48, 543-79 (1951). (Supply exhausted)

8. "The Chemical-Biological Coordination Center of the National Research Council". 26 pp. February, 1952. Describes the program and progress of the Center.

Note: Requests for volumes for which a charge is made should be directed to the Publications Office, National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C. Checks or money orders should be made payable to the National Academy of Sciences.

Requests for the indicated free copies should be directed to the Chemical-Biological Coordination Center, National Research Council, at the same address as given above.

USE OF THE CENTER'S FACILITIES

The assembly and organization of chemical-biological data are being carried out by the Center so that such data can be made readily available and hence utilized by scientists who need them. This applies particularly to representatives of the agencies which are providing funds for the Center's operations. The procedures developed by the Center greatly facilitate the ease of locating desired information which comes within its scope. The ability to locate easily such information becomes increasingly important as the output of scientific literature grows by leaps and bounds.

The Center will attempt to provide answers to submitted questions if:

1. The request is made by an authorized scientist, i. e. one associated with an educational, industrial, or governmental institution and the answer is required in connection with a laboratory or literature investigation.

2. The request concerns chemical-biological data or sources of chemicals needed in biological investigations. It should be noted that the Center does not prepare data sheets from articles concerned only with the synthesis of compounds nor from articles which report the results of biological studies in which chemicals are not used. Furthermore, the Center does not abstract articles which report biological data on ill-defined chemicals and mixtures. To merit abstracting the articles must describe the study of chemicals which are reasonably pure even though their structures may be unknown. The Center also does not abstract articles describing the normal metabolism of biological organisms or articles describing chemicals normally present in the diet or culture medium whose nutritive values are well established.

3. The request does not require the preparation of a complete bibliography. This limitation is imposed because the Center does not wish to compete with the services already provided by many libraries. However, in documenting the answers which the Center provides to the submitted questions a limited number of leading references will generally be given.

4. The request is clear, concise and not subject to misinterpretation. Thus, if the Center is requested to provide certain biological data on a given compound "and its derivatives" or "and its analogs", it is necessary that the questioner indicate the specific structures on which he desires information. This precludes an arbitrary decision by the Center as to which structures to include and exclude in the preparation of an answer. Similarly, a request for toxicity data should state, generically or specifically, the organism or organisms to be included in the search and the type of toxicological data desired.

Answers to many questions can be given by correspondence. The answer will generally include a brief statement summarizing the data contained in the Center's files plus a listing of the pertinent references. It is believed that most investigators prefer to study the original literature themselves and make their own interpretations of the data. If an answer is too complex and voluminous to permit its typing and mailing, the submitter of the question will be invited to visit the Center and make personal use of the files with whatever assistance is required of the Center's staff.

The completeness of the answers which the Center can at present provide to submitted questions is, of course, dependent on the number of journals which have been abstracted and coded, on the amount of data from the screening program which have been organized into the files and on other data from unpublished sources which have been made available. As mentioned on page 8 the Center is actively abstracting and coding data from about 45 carefully selected periodicals. January, 1946, was the arbitrarily selected date for the start of the abstracting-coding program and hence the Center's files do not, as yet, contain data which were published before this date. Some of the selected journals have been completely covered for the period 1946 to date, whereas others are in various stages of completion. During the current year special emphasis is being placed on abstracting and coding data in the fields of cancer, chemotherapy, entomology, microbiology and plant sciences. About ten general journals such as Nature, Science, Experientia and the leading chemical journals are being abstracted-coded and yield data in important fields in addition to those just mentioned.

It should be pointed out that during the five years since the Center was organized major effort was necessarily devoted to the development of codes and procedures. These developments have been completed and the Center can now concentrate on its abstracting-coding program which will result in the organization of an increasing amount of data in its files. Unless the data are used they serve no purpose. Consequently the Center invites scientists to submit questions, the answers to which will assist their research.