Retrieval System for Quality Control Drug Data*

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An information system for quality control drug data on punched cards is described. Computer programs employing an IBM System 360/30 permit selected organization and listing of alphanumeric data from 50 control operations involving approximately 500 raw materials and finished products. Certificates of analysis required for each product are prepared by the computer. In addition, a convenient review of out-of-limit test results is possible and statistical analyses are performed.

The need for a fast and reliable method of recording and retrieving different quality control drug data was recognized at the A. H. Robins Co. several years ago. Company growth and increased governmental controls necessitated processing a larger number of materials by quality control and an increased number of tests to be conducted on each material. In order to fulfill this requirement for processing data on materials passing through the quality control laboratories, many retrieval procedures were considered from the standpoint of the number and type of personnel and equipment available. In addition, the relationship of internal operations to potential external operations was considered. Such a relationship, involving use of internal and external data, should allow for both optimum control of product quality and ready access to information necessary for possible transmittal to Robins' subsidiaries and governmental organizations.

The quality control retrieval system, which we designed, involves the recording of data on punched cards and retrieval of information by means of a computer after transferring to magnetic tape. An IBM 360/30 computer is employed to process the desired data. Information from the laboratories recorded on punched cards is processed the same day and is available for retrieval purposes. The recorded data are then analyzed to indicate either acceptance or rejection of a material for routing to inventory or shipping.

Development of the semi-automated report system for quality control at the A. H. Robins Co. has progressed through three well-defined phases:

Definition of the objectives of the desired information system without regard to methods of implementation.

Development of an operational retrieval system by correlating objectives with available EDP equipment.

Expansion of the system through appropiate modifications to meet changing or unanticipated conditions.

The following nine objectives formed the basis for designing the quality control information system:

Record 5 to 15 test results per raw material.

Record 5 to 15 test results per finished product.

Process 2000 to 3000 samples each per year for both raw materials and finished products.

Minimize clerical recording and reduce time required for retrieval of data.

Provide capacity to organize and retrieve data received during a 5-year period.

Provide for fast recall of any of the data, either in part or in its entirety.

Produce printouts of analytical reports and certificates of analysis.

Arrange analytical data for future new drug applications.

Provide an expandable system which can be adapted easily for interdepartmental company needs.

Figure 1 illustrates the incorporation of these objectives into the quality control system for handling data from 75 finished products. A similar operational scheme is used for the more than 400 raw materials used to make these products.

To expedite the processing of data in the laboratory, the format of each punched card was designed so that quality control data could be written directly on the card in such a way as not to interfere with the subsequent keypunching operation. The identification and summary physical data cards illustrate two types of card formats employed.

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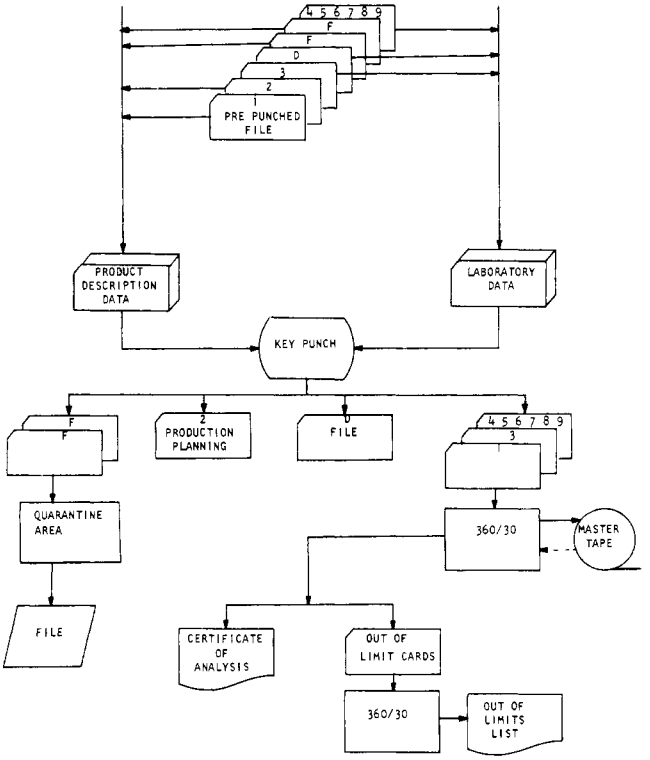


Figure 1. Finished products system

IDENTIFICATION CARD

Columns

1	Card identification
2–6	Date
7–8	Status (approval or rejection)
9–12	Product code
13–17	Control number
18–24	Lot number
25–27	Source (supplier)
28–37	Quantity
38–80	Accounting, stock, and contract designations

SUMMARY PHYSICAL DATA CARD

Columns

1–12	Area reserved for written test results (numbered lines correspond to tests designated and later keypunched in columns 22–80).
13–16	Product code
17–21	Control number
22–36	Weights (gross, fill, etc.)
37–46	Special tablet tests
47–52	Color tests
53–66	pH, refractive index, specific gravity, and optical rotation
67–69	Volume
70–72	Hardness
73–76	Defects
77–80	(Open)

Some data (product identification, lot number, etc.) are prepunched in the card prior to analyzing the sample in the laboratory. This approach permits ready access by laboratory personnel to punched cards required for recording data. After the results have been recorded, the completed cards are then approved or rejected by a supervisor and the data punched in the designated field on the card. The punched cards are sent to data processing where a taped program directs the selecting of card and tape information for subsequent printouts of certificates of analysis (See Figure 2).

In addition to the certificates of analysis for domestic products, certificates are made available for government agencies and many foreign sources that submit samples to Richmond for analysis. Another interesting point concerns a by-product of the certificate of analysis. The computer has been programmed to provide a separate listing of all out-of-limit test results. This list is particularly helpful as it serves as a final review of physical-chemical data prior to the use of raw materials and prior to the packaging of finished dosage forms.

The computer program (available on request) was devised primarily for the automatic printout of copies of certificates of analysis. Test results are analyzed to determine if the results are within prescribed test specifications or out-of-limits. Test results are punched in cards and computer lists prepared for subsequent review. Computer listings of physical and analytical test data according to lot number and product code have been compiled, and statistical analyses of test results performed. Further, the computer program will accept alphanumeric codes designated by the laboratory analysts and translate

A·H·ROBINS | **Certificate of Analysis**

(A DECLARATION OF POTENCY AT TIME OF ASSAY)

To:
Product: DIMETANE TABLETS
Stock No:
Contract No:
Robins Code: DM

Lot. No: 213
Quantity: 1,134,106 TAB
Control No: 50739
Source: AHR
Assay Date: 6-01-67

Test	Specification	Result
APPEARANCE	UNCOATED TABLET, PEACH COLORED, ROUND, 5/16 IN DIAMETER, FLAT FACE, BEVEL EDGE, ONE SIDE MONOGRAMMED AHR, OBVERSE SCORED	UNCOATED TABLET, PEACH COLORED, ROUND, 5/16 IN DIAMETER, FLAT FACE, BEVEL EDGE, ONE SIDE MONOGRAMMED AHR, OBVERSE SCORED
WEIGHT USP	THEORETICAL 205 MG MAXIMUM 220 MG MINIMUM 189 MG	203 MG 215 MG 200 MG
HARDNESS	4.0 TO 11.0 KG	4.3 KG
DISINTEGRATION USP	LESS THAN 30 MINUTES	03 MIN
BROMPHENIRAMINE MALEATE IDENTITY	3.8 TO 4.2 MG POSITIVE	4.0 MG POSITIVE

A. H. Robins Company, Inc.
Quality Control Laboratory
1407 Cummings Drive
Richmond, Virginia 23220

This information is certified to be correct

Approved by: D. A. Mefford

Figure 2. Certificate of analysis

into complete words or numeric characters in the appropriate printout.

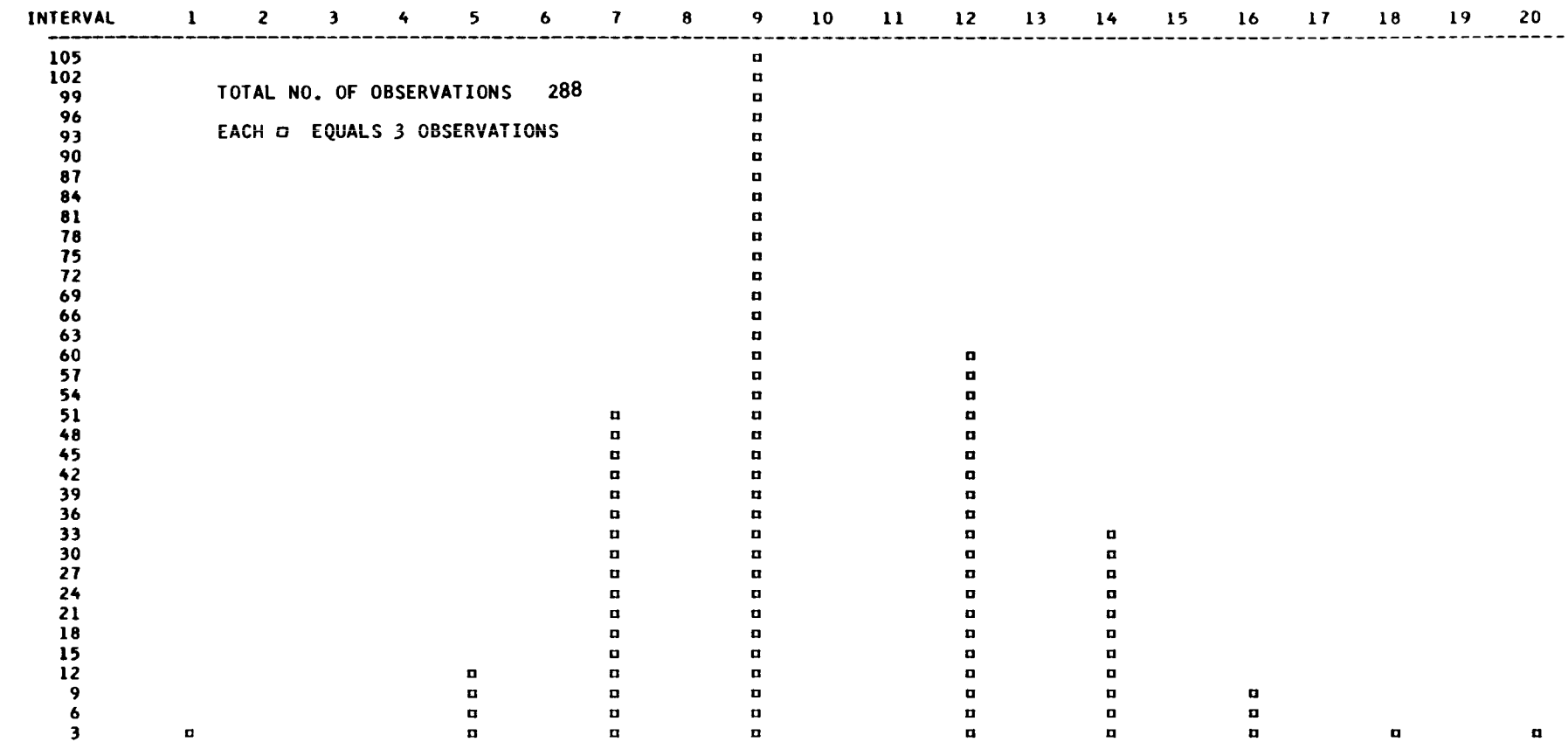
Frequently, the statistical analysis of chemical and physical data of a specific test is desirable. Experience has shown that the clerical effort involved in the accumulation of the necessary data to determine mean deviation, averages, high values, low values, and frequency distribution is quite time-consuming and laborious. The computerized histogram for pyridoxine hydrochloride (see Figure 3) is an example of a type of statistical analysis that is readily obtained.

Computer recall of analytical results arranged according to lot number produces a printout similar to the table shown in Figure 4 for phenobarbital. When vertical lines are drawn at the points of maximum and minimum limits, the out-of-specification results are easily observed. The computer program allows for recording results in increments of 0.1 mg.

The use of the keypunched data in the finished product identification cards has proven to be of significant value for end-of-year inventory. Listings of each of 75 different finished products in a manner similar to Figure 4 minimizes clerical time while providing clearly printed summaries of required data. Also, monthly tabulations of raw material

Lot Number	Minimum 15.4 Mg. Per Tablet	Maximum 17.0 Mg. Per Tablet
3246		+
3247		+
3248		+
3249		+
3250		+
3251		+
3252		+
3253		+
3254	+	
3255	+	
3256	+	
3257	+	
3258	+	
3259	+	
3260	+	
3261	+	
3262	+	
3263	+	
3264		+
3265		+
3266		+
3268		+
3269		+

Figure 3. Histogram of pyridoxine hydrochloride



INTERVAL	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
FREQUENCY	3	0	2	0	12	0	52	0	107	0	0	61	0	34	0	11	0	3	0	3
	3	3	5	5	17	17	69	69	176	176	176	237	237	271	271	282	282	285	285	288
PER CENT	1.0	0.0	0.7	0.0	4.2	0.0	18.1	0.0	37.2	0.0	0.0	21.2	0.0	11.8	0.0	3.8	0.0	1.0	0.0	1.0
	1.0	1.0	1.7	1.7	5.9	5.9	24.0	24.0	61.1	61.1	61.1	82.3	82.3	94.1	94.1	97.9	97.9	99.0	99.0	100.0

Figure 4. Analytical results—individual lots of phenobarbital

purchases, approvals, or rejections have been an invaluable aid to the purchasing and manufacturing departments. In addition, the relationship between tablet hardness and disintegration rate has been statistically reviewed using results from samples extending over several years' production.

With the large amount of both chemical and physical data recorded in retrievable card form, other similar comparisons and evaluations of physical and chemical properties, production analyses, and product reviews are being considered and are expected to provide much useful information in the future.

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Indexing Polymers by Formula

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Information about polymers is indexed for retrieval by using the formulas of repeating units in polymers. A set of rules is proposed for indexing polymers and copolymers by formula. Examples illustrate each rule. The rules are consistent with the Wyandotte-ASTM codes for indexing spectral data on punched cards. The proposed system can handle organosilicon polymers, which may have fractional atoms in the repeating units.

Our spectroscopy laboratory must be able to locate reference spectra quickly. It is easy to find spectra of *compounds;* nearly everyone locates them by molecular formula written according to the rules of Chemical Abstracts Service (CAS). It has not been so easy to find *polymers* this way. Homopolymers can be indexed under the formula of the simplest repeating unit. But it is not clear how copolymers are to be indexed, or how to handle organosilicon polymers which often have fractional atoms in the repeating units. This paper describes the system we worked out for indexing polymers by formulas.

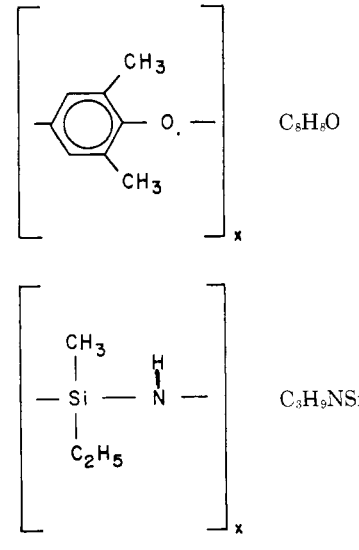
Three major convictions guided the development of our polymer-indexing system:

> The system should use the same order of symbols in formulas as does CAS (*1*).
>
> The system should be a logical extension of the American Society for Testing and Materials' Wyandotte-ASTM rules for indexing spectral data on punched cards (*2, 3*).
>
> The system should be compatible with the shorthand designation for siloxane units in silicone polymers (*4, 5*).

Starting from these principles, we developed a systematic set of rules for indexing polymers by formula. These rules are illustrated in the following examples:

Homopolymers. Homopolymers (polymers containing a single type of unit) are indexed under the formula of the smallest repeating unit.

Examples:



The arrangement of symbols in formulas follows CAS rules (*1*).

Copolymers Having Two Kinds of Repeating Units. Copolymers are considered to have a 1:1 molar ratio of the two kinds of units, regardless of the actual ratio in the copolymer. In the examples below, each copolymer