1972

Organization and Development of a Computerized Drug-Drug Interaction File

Charles Daniel Mahoney
University of Rhode Island

Follow this and additional works at: <https://digitalcommons.uri.edu/theses>

Recommended Citation

Mahoney, Charles Daniel, "Organization and Development of a Computerized Drug-Drug Interaction File" (1972). *Open Access Master's Theses*. Paper 203.
<https://digitalcommons.uri.edu/theses/203>

This Thesis is brought to you for free and open access by DigitalCommons@URI. It has been accepted for inclusion in Open Access Master's Theses by an authorized administrator of DigitalCommons@URI. For more information, please contact digitalcommons-group@uri.edu.

ORGANIZATION AND DEVELOPMENT OF A COMPUTERIZED

DRUG-DRUG INTERACTION FILE

BY

CHARLES DANIEL MAHONEY

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE

REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

IN

PHARMACY

UNIVERSITY OF RHODE ISLAND

1972

MASTER OF SCIENCE THESIS
OF
CHARLES DANIEL MAHONEY

Approved:

Thesis Committee:

Chairman

Joan M. Laurie
Robert J. Donaherty
Norman R. Campbell
Anthony N. Pernita

A. G. Michel
Dean of the Graduate School

UNIVERSITY OF RHODE ISLAND

1972

TITLE ABSTRACT

COMPUTERIZED DRUG-DRUG INTERACTION FILE

ABSTRACT

The project was designed to organize and develop a computerized drug-drug interaction file. The methodology for the organization, storage and retrieval of drug-drug interaction information is discussed. In order to accomplish this objective several requirements were met. They are as follows: (1) Selection and evaluation of clinically significant drug-drug interactions from the scientific literature, (2) Creation of a computerized data bank for drug-drug interactions, and (3) Design and development of a computerized printout which reports the information in concise summaries.

The file is designed to be compatible with existing computerized record keeping and drug information systems. In addition, the retrieval system has several unique characteristics. The reporting format is designed to provide practical drug-drug interaction information in a concise summary which can be easily understood and utilized by either a physician or pharmacist in a patient care environment. It will provide the clinical pharmacist with a invaluable reference to be utilized as a "key" to clinical involvement with the medical staff. The printout may be incorporated into a patient's cumulative medication profile or merely used as a reference source to screen for probable drug-drug interactions. Another unique feature of the system is that it reports important drug-drug interactions with each drug entity the patient is receiving. The system is not limited

to the reporting of specific interactions which may occur with the patient's current therapeutic regimen.

Several illustrations are presented using the file in conjunction with a computerized medication profile system. The applications of this system provide a rational approach towards determining the probability of drug-drug interactions resulting from the concurrent administration of drugs.

ACKNOWLEDGEMENT

The author wishes to thank Dr. Joan M. Lausier and the members of the thesis committee for their assistance in editing this manuscript. The author is especially grateful to his wife, Carolyn, for her untiring effort in the preparation of this manuscript and to Mr. Paul-Emile B. Platiau for his advice and programming assistance.

TABLE OF CONTENTS

	PAGE
ABSTRACT	iii
ACKNOWLEDGEMENT	v
TABLE OF CONTENTS	vi
LIST OF ILLUSTRATIONS	vii
I. INTRODUCTION	1
II. METHODOLOGY	8
III. RESULTS AND DISCUSSION	13
IV. CONCLUSIONS	34
V. REFERENCES CITED	36
VI. APPENDICES	40
I. Source Document	40
II. Alphabetical Cross-Index	64
III. Message Code Index	69
IV. Selected References	75
V. Drug-Drug Interaction Printout	94
VI. Computer Program	111

LIST OF ILLUSTRATIONS

ILLUSTRATION	PAGE
I. Patient Medication Profile. Example I	27
II. Patient Medication Profile. Example II	30

I. INTRODUCTION

In the last several years there has been an increasing awareness of drug interactions in the medical and pharmaceutical literature. The recognition of drugs that interact with other drugs is of more than passing interest because of the potential consequences of unpredicted reactions.

The phrase "drug interactions" is now part of the common terminology used in medicine and pharmacy. The phenomenon of drug interactions includes the interaction of drugs with certain foods, laboratory tests, and various underlying pathological states. The scope of this project is restricted to drug-drug interactions.

Drug-drug interaction is a phenomenon which occurs when the effects of one drug are altered by the prior or concurrent administration of another (or the same) drug (s). It presents a complex and profound problem. The means by which drug interactions occur are varied and complex. They may arise either from alteration of the absorption, distribution, biotransformation or excretion of one drug by another, or from a combination of their actions or effects.

In order to have a general understanding of drug interactions one must have a basic knowledge of a number of mechanisms. The basic causes for these interactions are as follows:

1. Potentiation

Drugs having similar pharmacological properties can

be expected to potentiate one or more of the pharmacological effects in patients taking these medications.

2. Antagonism

Drugs which have opposing pharmacological effects may produce a combined effect less than that of the active compound. The basic underlying mechanism of drug antagonism may be chemical, competitive, non-competitive or physiological.

3. Alteration of Gastrointestinal Absorption

Drugs may alter gastrointestinal absorption by complexation or by changing the pH of the gastric fluid. Since many drugs are weak acids or bases, the pH of the gastrointestinal tract will influence the extent of absorption and also the site at which absorption takes place. Drugs may form inactive or insoluble complexes with other drugs in the gastrointestinal tract. It is well known that tetracyclines can combine with di- and trivalent cations to form a complex which is poorly absorbed.

4. Stimulation of Metabolism

A number of drugs can increase the activity of liver microsomal enzymes. The enzyme stimulation results in a more rapid metabolism and excretion of other drugs

that are simultaneously administered.

5. Inhibition of Metabolism

Drugs that can inhibit the activity of liver enzymes indirectly may increase the activity of drugs which depend on this enzyme for their metabolism.

6. Displacement of Drugs from Protein Binding Sites

A competition will exist when two or more drugs are administered concurrently which are capable of binding to proteins. The drug that has the greater affinity for the binding site will displace the other from the plasma or tissue proteins.

7. Interactions at the Receptor Site

Some drugs combine with receptors to form complexes that elicit responses (agonists). Other drugs combine with receptors and elicit no responses (antagonists). In this type of interaction the degree of response will depend on the drug and its affinity for the receptor site.

8. Alteration of Electrolyte Levels

Changes in electrolyte levels may make certain physiological systems more sensitive to the effects of a particular drug.

9. Alteration of Urinary Excretion

Alteration of urinary excretion can be accomplished by

changing the urinary pH or by interfering with tubular excretion. The renal tubular reabsorption of a drug can therefore be increased or decreased by another agent.

The economic consequences of drug reactions are staggering. It has been reported that one seventh of all hospital days are devoted to the care of drug toxicity, at an estimated yearly cost of three billion dollars (1). Considerable attention has been focused on the increasing incidence of drug reactions. Approximately 18 to 30 percent of all hospitalized patients experience a drug reaction during their hospitalization (2). In addition, 3 to 5 percent of all admissions to hospitals are primarily due to an adverse drug reaction (2, 3).

It is a difficult and cumbersome task for a hospital pharmacist to accurately review all medication profiles on a routine basis for drug interactions. Hospital pharmacists in the past (4, 5, 6) have attempted to meet this challenge by developing charts and card files specifically designed for the rapid retrieval of drug interaction information. However, this is an extremely time consuming task. Often it is a retrospective review rather than a prospective analysis. This situation has created a growing interest as well as a potential need for more efficient electronic data processing (EDP) methods designed for the retrieval and utilization of documented drug-drug interactions.

Another factor creating an interest in the field of drug inter-

actions is the potential liability of the pharmacist and physician. The failure to avoid or notice a potentially harmful effect resulting from a drug-drug interaction can make either the physician or pharmacist a candidate for liability. If screening a patient's medication profile is a duty pharmacists accept in a particular locale, then this will undoubtedly become part of the standard of care for patients in that area (7). When such is the standard of practice the public will expect the pharmacist to perform this function carefully and prudently.

This project was undertaken to organize and develop a file of drug-drug interaction data suitable for computerization. In order to accomplish this objective several requirements were met. They are:

1. Selection and evaluation of clinically significant drug-drug interactions from the scientific literature.
2. Creation of a computerized data bank for drug-drug interactions.
3. Design and development of a computerized printout which reports the information in concise summaries.

The scientific literature is replete with relevant clinical studies (8, 9, 10, 11) and isolated case reports (12, 13, 14, 15) citing drug-drug interactions. The National Library of Medicine's computer-based Medical Literature Analysis and Retrieval System (MEDLARS) compiles and produces Toxicity Bibliography which covers the adverse and toxic effects of drugs reported in approxi-

mately 2,300 biomedical journals. This reference is similar to other indexing and abstracting services in that they are all designed to provide a means to access the scientific literature pertaining to chemical and biological interactions. Services such as this are an important contribution towards realization of a comprehensive toxicology information system; however, they only constitute the initial phase in developing a mechanism which provides the clinician with drug-drug interaction data in a practical "ready to use" format.

Multiple-drug administration is common to both hospitalized and ambulatory patients. It is extremely common for a patient to be suffering from more than one unrelated disorder which demands simultaneous treatment with two or more drugs. In such instances interactions are often unexpected. Melmon (1) reported that the average patient in a hospital receives six to ten drugs during his hospitalization. At this level of multiple-drug administration, the adverse reaction rate was reported to be 7 to 10 percent. Some patients receive more than 20 drugs simultaneously. Under such circumstances the patient has at least a 40 percent chance of having adverse reactions to one or more of the drugs. Multiple-drug therapy generally provides greater efficacy than can be achieved with full doses of single drugs, greater margin of safety, or more satisfactory onset or duration of effect. In addition to the administration of drugs concurrently for their independent and unrelated effects,

drugs are sometimes administered concurrently to make use of expected interactions. The phenothiazines markedly affect the actions of a number of other drugs. Phenothiazines are often prescribed for their ability to potentiate the effects of central nervous system depressants. It is common practice to administer a phenothiazine such as promethazine hydrochloride concurrently with a narcotic analgesic in order to reduce the dosage of the narcotic that would normally be required to produce the desired level of analgesia.

II. METHODOLOGY

The scientific literature, both primary and secondary reference sources, was reviewed and evaluated for clinically significant drug interactions. Only drug-drug interactions reported in humans are included in this compilation. Drug interactions occurring only in animals or only in vitro systems have been excluded.

EVALUATION PROCEDURE:

In the assessment of drug interactions for this compilation a selected number of original references were reviewed and evaluated. Secondary references (eg. review articles, drug interaction tables, manuals, etc.) generally do not provide sufficient information on which to make an evaluation. Secondary references are useful in cross-indexing closely related drugs but not, of the same group mentioned in the primary reference source. This is an extremely complex problem since for every basic drug class (eg. barbiturates, corticosteroids, sulfonamides) there are many similar generic drugs which closely resemble the parent compound. In order for a drug interaction compilation to be of any practical value the structure activity relationships of these various compounds have to be taken into consideration. Secondary reference sources were first evaluated on the content of the discussion and the references they provided the user before any decision was made concerning the validity of a particular drug-drug interaction listed in the text.

The initial undertaking was to review a number of abstracting and indexing services, which included, Toxicity Bibliography, International Pharmaceutical Abstracts, Clin-Alert, and FDA: Clinical Experience Abstracts.

In the evaluation of the primary literature for reports of drug interactions the following journals were consulted whenever possible:

1. American Journal of Psychiatry
2. Annals of Internal Medicine
3. Clinical Pharmacology and Therapeutics
4. British Journal of Anesthesia
5. British Medical Journal
6. Anesthesia and Analgesia
7. New England Journal of Medicine
8. Lancet
9. Neurology
10. Journal of Pediatrics

Isolated case reports were only considered if there was some conclusive documentation cited in the literature. Generally speaking, it is extremely difficult if not impossible, to differentiate a case report of a suspected drug interaction from a idiosyncratic or hypersensitive reaction attributable to one of the active components in the multi-drug therapy. What further complicates a literature search for drug interactions is that there are few accepted scientific

studies. The well-controlled clinical experiment is virtually non-existent for obvious reasons. It is difficult for a practitioner to justify re-challenging a patient to a drug when a drug interaction is suspected. Especially if there are other drugs or therapeutic measures available to treat the condition. When there was a choice of references a number of criteria were used to evaluate the study. The general requirements for an adequately controlled study are an objective and practical (sensitivity) method of evaluation, an adequate number of subjects, lack of bias, concurrent comparison of the drug regimen in question with a reference standard, dosage variance, and appropriate statistical validation.

EVALUATION CRITERIA:

There are many factors which may modify the effects of drugs. Some of these result in qualitative differences in the effects of a drug while others produce only quantitative changes in the effects of the drug which are dose dependent. It is extremely important to evaluate a number of specific patient factors before an adverse response is attributed to a drug-drug interaction. The physiological, pathological and genetic factors which are well known to alter response to drugs and which were taken into consideration are age (infant and elderly), sex, race, body weight (nutritional state), tolerance, pathological state, metabolic differences and organ function. The specific mechanisms for these physiological states altering drug response

are well documented in the literature (16, 17).

Another area of paramount importance is the variables associated with drug dosage and route and method of administration. Specifically these factors can be categorized as dosage, route of administration, dosage form, frequency of administration and duration of therapy.

In any defined population, response to a drug generally follows a normal distribution. That is, a few patients will be hypersensitive and will respond to a small dose while a large majority will respond best in the therapeutic range. On the other hand, a few will be relatively resistant to the effects of the drug. This kind of response curve applies to both therapeutic effects and adverse responses which may include drug-drug interactions.

There are a number of parameters which proved helpful in determining the clinical importance of reported drug interactions. They are: occurrence (animal or human, in vivo vs. in vitro), incidence, etiology, structural activity relationships, severity of reported interaction, clinical manifestations, clinical course, prognosis and treatment.

FORMAT AND INDEXING:

This computerized drug interaction file is designed to be compatible with a number of existing computerized record keeping and drug information systems. The information in the file provides a

concise pharmacological summary in a reporting format suitable for actual clinical use in the patient care environment.

The specific drug entities are cross-indexed to a message code. The message code was assigned from a listing of valid numbers calculated by $(5A + 4B + 3C + 2D + E) / 11 = Y \times 11$. The source document (reference document) which consists of the message codes, arranged sequentially, and the appropriate drug interaction summary was then compiled. In the source document the interactions enumerated in the summary or message are coded to one or more specific references. This particular coding system offers the user a means to obtain the specific references on which the information in the message is based.

Combination products in the top two-hundred prescribed drugs are included if one or more of the active ingredients was implicated in a drug interaction. For example, Desbutal-15 Gradumet which contains methamphetamine hydrochloride 15 mg. and pentobarbital sodium 90 mg. is assigned two different messages. The messages for barbiturates and amphetamines will be reported when the file is searched for possible drug-drug interactions involving this combination product.

III. RESULTS AND DISCUSSION

The system is designed to provide the physician with important drug information on selected drug-drug interactions. In addition, and equally as important, it will provide the clinical pharmacist on the Patient Care Unit with a valuable reference to be utilized as a "key" to clinical involvement with the medical staff. The basic objective of the system is to provide the physician and clinical pharmacist with a reference source enabling him to rapidly screen a medication profile for possible drug-drug interactions. When a probable drug-drug interaction is noted, and it is definitely determined the patient is receiving both medications concurrently the clinical pharmacist may then elect to contact the physician. In certain instances it may be only necessary for him to inform the nurse of the possible interaction. For example, if a patient is receiving both an antacid preparation and bisacodyl tablets, an enteric coated laxative, the pharmacist should advise the nurse not to administer both medications simultaneously, but rather as far apart as possible.

A source document (reference document) was the first document compiled (Appendix I). A five character numeric code was assigned to each message. The specific drug entities which were coded in the source document were compiled and cross-indexed to the respective message code (Appendix II). A second index (Appendix III) was compiled listing the message codes in sequence and the par-

ticular drugs to which the summary applies. This index is useful to the user when it is necessary to determine the complete list of drugs which have been indexed to any one particular message. The source document codes the specific interaction enumerated in the summary to one or more specific references thereby offering the user a means to obtain the references on which the information is based. A list of the selected references utilized is included (Appendix IV).

A printout of the messages exactly as they were retrieved from storage is included for illustrative purposes (Appendix V). The printout included in this document represents a xeroxed copy of a computer printout which was photoreduced by twenty percent.

The following message represents an example of a summary as it was printed from the data bank:

Salicylates elevate the anticoagulant response to oral anti-coagulants, increase plasma levels of unbound penicillin G and derivatives and potentiate methotrexate and sulfonyleureas. Salicylate plasma levels may be decreased by corticosteroids. They may decrease serum levels of indomethacin (Indocin) and inhibit uricosuric activity of sulfinpyrazone (Anturane) and probenecid (Benemid).

If the information is of interest to the physician hopefully he will be stimulated to seek the references and request a "consultation" from the Pharmacy for further evaluation. A pharmacy consultation would consist of a pharmacist reviewing a patient's medical record in light of the drug-drug interaction information reported for a particular patient. The pharmacist would determine if the drug-drug

interaction information is significant in that patient and whether the patient's physician should be informed of the findings. In order to accomplish efficient retrieval of the specific references which were applicable to the message, a source document (reference document) was created (Appendix I). Ideally it would be advantageous to create a file containing the hard copy of the references most frequently requested. As the number of references increase the original copy can be microfilmed and placed in a microfiche to reduce storage requirements. The previous example appears in the source document as:

04383 Salicylates

Salicylates elevate the anticoagulant response to oral anti-coagulants (13), increase plasma levels of unbound penicillin G and derivatives (14) and potentiate methotrexate (16) and sulfonylureas (17). Salicylate plasma levels may be decreased by corticosteroids (15). They may decrease serum levels of indomethacin (Indocin) (53) and inhibit uricosuric activity of sulfinpyrazone (Anturane) (18) and probenecid (Benemid) (19).

Generally speaking, the reference selected for the list (Appendix IV) represents the most scientific and significant literature citation reviewed for that particular interaction. In certain instances two or more references are cited for a specific interaction. When more than one mechanism has been postulated in the literature a cross sample of references are included. For example, salicylates have been shown to displace methotrexate from plasma protein binding, thereby elevating plasma levels of free methotrexate. However,

salicylates may also block the renal excretion of methotrexate. Therefore the increased activity of methotrexate, usually manifested by increased toxicity, is attributable to both of these mechanisms.

REPORTING FORMAT:

The reporting format is designed to provide practical information in a concise summary which can be easily understood and utilized in a patient care environment. The printout may be incorporated into a patient's cumulative medication profile or used strictly as a reference source to screen for drug-drug interactions.

A reporting format (previously illustrated) was chosen which would enable a physician or a pharmacist to effectively review a patient's previous medication history as well as the present drug therapy for suspected drug-drug interactions. A unique advantage of this system is that it reports important drug-drug interactions with each drug entity the patient is receiving. The system is not limited to the reporting of specific interactions with the concomitant use of two drugs.

A retrospective review of a patient's previous medication history is a valuable exercise in light of the extended biological half-life of many drugs and the many structural similarities which exist. This is extremely important since so many of the reported drug interactions exhibit structure activity relationships and are not specific for any one drug entity. The sulfonamides are a class of drugs in

which a number of the drug interactions involving these compounds are structure dependent. This information is of practical value in a patient care environment, because it provides the physician with drug interaction information which will enable him to make an intelligent choice as to the appropriate class of drugs to prescribe.

This sort of information is also helpful in predicting unknown reactions which may occur with new drugs. There are many instances when it is impossible to predict a possible drug-drug interaction based on the structure activity relationship to a parent compound. For example, a new drug with a phenothiazine nucleus would be expected to potentiate the effects of central nervous system depressants. In the majority of instances so-called new drugs are merely molecular modifications of an existing generic drug or are compounds which are transformed to a pharmacologically active compound which in itself is commercially available.

The importance of knowing beforehand when two drugs given together will result in an interaction cannot be overemphasized. Since drug interactions unknown to-date cannot be predicted in patients taking two or more drugs at the same time, only those interactions already reported in the literature offer any clue as to what drugs make a rational combination.

LITERATURE EVALUATION:

Drugs which exert a similar pharmacological action and which

are prescribed for the same therapeutic purposes were not considered as examples of drug-drug interactions having additive or synergistic pharmacological effects (e.g. epinephrine and levarterenol). Another broad area which was not included in this file is the rationale of combining both bacteriostatic and bactericidal antibiotics in the same therapeutic regimen. Jawetz (18) has reported that antibiotic antagonism may occur but the net effect plays a minor role in clinical medicine. This has been an extremely controversial subject for years and still has not been resolved. The inclusion of this sort of material in a drug interaction compilation is of no practical value.

One of the major difficulties in evaluating drug interactions is the occurrence of contradictory reports concerning a specific interaction. For example, a drug interaction of considerable interest to neurologists is the reported inhibition of diphenylhydantoin and phenobarbital metabolism by methylphenidate. Recent studies (19, 20) indicate that during the period of concurrent drug administration there is no elevation in diphenylhydantoin plasma levels or clinical signs of drug toxicity. Based on the results of these two studies this suspected interaction was not included in the file. Although these studies do not preclude the possibility of an interaction of methylphenidate with the anticonvulsants they do suggest that if this interaction does exist it must occur infrequently.

A similar case is illustrated by the combination of a tricyclic

antidepressant and a monoamine oxidase inhibitor (MAOI) in the treatment of depression. This combination is often contraindicated in the literature as well as the respective product brochure. In certain instances a medication-free period of two weeks is recommended after discontinuance of the MAOI and the institution of a tricyclic antidepressant. However, there have been two recent publications (21, 22) concerning antidepressant therapy which indicate that the combined use of a tricyclic antidepressant and a MAOI may not be hazardous and that this method of treatment may be used with considerable benefit to the patient. Since it was listed as a caution in the product brochure it was decided to include it in the files despite the fact that the clinical significance of this interaction has not been demonstrated.

The interaction between chloral hydrate and warfarin sodium is even more complex. In 1966 Cucinall et al (23) suggested that the coadministration of bishydroxycoumarin and chloral hydrate resulted in a reduction in expected plasma levels of the anticoagulant with a decrease in prothrombin time. Sellers and Koch-Weser (24) showed that the administration of 1 Gm. chloral hydrate for one week increased the hypoprothrombinemic effect of warfarin sodium by 40 to 80 percent. Griner, P.F., et al (25) recently conducted a study to determine the effect of chloral hydrate in patients receiving long-term therapy with warfarin sodium. Their findings, unbelievable as

they may seem, indicated that chloral hydrate or its equivalent as chloral betaine, in doses of 0.5 to 1 Gm. daily, did not influence the anticoagulant effect of warfarin in such patients. Since the studies reported in the literature are not conclusive and the results remain contradictory it was decided to include in the file a statement to the effect that "chloral hydrate variably effects the anticoagulant response to oral anticoagulants." This statement merely points out the fact that chloral hydrate may in some way interfere with the hypoprothrombinemic effect of oral anticoagulants.

Diphenylhydantoin is one of many drugs metabolized by enzymes found in the microsomal fraction of hepatic cells. The drug phenobarbital, is known to stimulate these enzymes and thus the metabolism of diphenylhydantoin. Apparently, the ability of phenobarbital to lower plasma levels of diphenylhydantoin is not so great as to offset its own anticonvulsant activity. Although a biochemical antagonism exists the net result is a potentiation of the desired pharmacological effects. This particular combination is the drug regimen of choice for grand mal epilepsy. A suspected or reported drug interaction can not be evaluated solely on the basis of biochemical data. It must be remembered that combination drug therapy attempts to achieve one or more therapeutic effects with a minimum of adverse effects. The ultimate clinical objective of the therapeutic regimen must always be considered. On the other hand, this antagonism may be significant if the patient

was receiving large doses of diphenylhydantoin (common to hospitalized patients in psychiatric hospitals) and then had the phenobarbital discontinued. In this particular case, the diphenylhydantoin plasma levels may well rise to a toxic level.

Isolated case reports (one or two patients) were excluded except the reports concerning methotrexate and small pox vaccination. Methotrexate, a antineoplastic agent, may inhibit the immunological response to smallpox vaccine resulting in generalized vaccinia. The decision to include this interaction was strictly subjective and not based on any rational scientific data. Regardless of the severity of the reaction one would not expect to find numerous cases or controlled studies since the use of this combination is very limited. An important consideration is that by reporting this interaction it may alert the prescriber to possible difficulties with other immunosuppressive drugs, namely the corticosteroids.

There are a number of interactions which are well known in medical circles but specific clinical documentation is lacking. The major area of concern to the clinician is that although the clinical data is lacking they are included in the pharmaceutical brochure which brings about a potential legal liability. From a medicolegal standpoint it is wise to include these in a drug interaction file in order that the physician will be forewarned about a possible adverse effect. If the drug interaction is included in the product literature

as a caution or warning the physician is faced with a legal dilemma. In this situation the physician may wish to select another drug or decide to run the risk to the patient. This situation is applicable to the following examples of drug-drug interactions: Propoxyphene-orphenadrine, meperidine-isoniazid, and allopurinol-iron.

CURRENT APPLICATIONS:

The system is designed in a manner which enables it to be incorporated into a program using computerized medication profiles. The messages or supplementary notes pertaining to possible drug-drug interactions immediately follow the cumulative medication profile (Illustration I). In the first example (Illustration I) the information presented in the accompanying messages does not suggest any specific drug interactions with the drug regimen outlined in the medication profile. However, the information would be extremely useful to the physician if he were considering adding additional drugs to the present therapeutic regimen. The information previously presented may forewarn him of an interaction. In the second example (Illustration II) the messages describe pertinent drug-drug interactions which are possible with the current therapeutic regimen. If a medication has been discontinued the drug interaction summary is not printed. This check is built into the computer program. For example, in Illustration I the message summary for diphenhydramine hydrochloride (an antihistamine) was printed while it was not in the

second illustration since the drug had been discontinued.

The program of instructions designed to print the cumulative medication profile and search the drug interaction file for the appropriate drug interaction message code is included (Appendix VI). The computer program is written in COBAL.

From a practical viewpoint it is difficult to justify a computer program which does not always produce a tangible result. It is much more difficult to implement a program limited to professional objectives as opposed to a cost accounting program designed to process medication charges. As with most organizations computer time is expensive and is limited. An additional feature of the cumulative patient medication profile described in this project is that it can be used as a dispensing record for a medication distribution system.

All that is necessary to incorporate this file into an ongoing computerized system is to place the file in storage and then assign message codes to drug names listed in a computerized drug product file or a drug data file. In order to facilitate this task the specific generic entities are cross-indexed to the appropriate message codes (Appendix II). The drug product file can be compiled by the individual institution or a commercially available file can be purchased. The American Society of Hospital Pharmacists Drug Product Information File (DPIF) serves as a master drug code dictionary and is adapt-

able to each individual system. The DPIF is a data bank composed of terms and code numbers for commercially available drug products which is organized to facilitate automated processing of drug data. This particular multi-functional drug coding system is based on a 5-digit generic drug product number that completely identifies the generic drug product.

Retrieval may be accomplished by one of two basic methods: (1) As an integral component of a computerized medication profile and/or pricing system. (2) Manual selection of pre-punched cards.

The file can be easily utilized by individuals who do not have a computerized profile system. They can create a tub file of pre-punched index cards and then select the applicable cards upon special request. A prospective review of drug interactions can then be conducted by running a program to search the file in storage. A system similar to this is utilized by the Drug Information Center, Mercy Hospital, Pittsburgh, Pennsylvania (25).

FUTURE APPLICATIONS:

It is possible to prepare a manual from the drug-drug interaction file. This aspect of the system would be especially useful to individuals without access to electronic data processing facilities. This would serve as a supplementary reference source which would enable the user to rapidly screen a medication profile in lieu of a computerized system. Under certain circumstances a request for

an immediate computer search is impractical, e.g. servicing a drug information request VIA the telephone or while participating in work and teaching rounds. The major sections, namely, the Source Document, Indexes, and Selected References can be cross-indexed, typed and then photoreduced.

Another valuable application of this file is that a drug-induced laboratory test interference file can be used in conjunction with the present system or incorporated into it. Drugs may possess the inherent ability to alter laboratory test values through a variety of pharmacological, physical or chemical mechanisms (27). A drug may affect the normal physiological levels of the particular substance being measured. Through physical or chemical interference, a drug may not only alter a test's value but may prevent its determination by a particular method. The extended biological half-life of drugs as well as intermediate or end products of drug metabolism may often be responsible for unsuspected alteration in laboratory test values. The reporting format and retrieval system is compatible with a program conducted by the Pathology Department of the Rhode Island Hospital, Providence, Rhode Island (28) for reporting possible drug-induced modifications of laboratory test values. In this particular program a computerized cumulative report of all laboratory tests is prepared for every patient who had a test conducted. Immediately following the cumulative report are supplementary

notes pertaining to drug-induced laboratory interferences for the tests outlined in the report. Although it is ideal to include this information in a cumulative laboratory report there are instances when this may not be practical and it would be preferable to include this information in the medication profile. A prime example would be a situation where a patient obtains health care services from an ambulatory patient care facility. Usually after the initial battery of laboratory tests only a few tests, if any, are conducted for continued surveillance of a particular physiological parameter. In this situation, it would not be economically feasible to run a specific program for laboratory tests.

The file is compatible with existing computerized drug information services. Another advantage of this type of drug-drug interaction file is that its use is not limited to an institutional setting. The system may be incorporated into a computerized drug information service coordinated by a regional drug information network and offered to community practitioners on a subscription basis VIA on-line computer terminals.

ILLUSTRATION I

Patient Medication Profile. Example I

MODERN HOSPITAL

DEPARTMENT OF PHARMACY

CUMULATIVE MEDICATION PROFILE FOR KAREN SMITH

		NO. 6572810	ROOM 602	AGE 26	
START	STOP	MEDICATION ORDERED			PHYSICIAN
2/08		DIAZEPAM 5 MG. PO TID PC			ALLEN
2/08		LITHIUM CARBONATE 0.3 GM. PO TID PC			CAMPBELL
2/08		ISOCARBOXAZID 10 MG. PO TID			CAMPBELL
2/10		SULFISOXAZOLE 0.5 GM. PO TID			STEINBERG
2/11		DIPHENHYDRAMINE HCL 50 MG. PO HS PRN			CAMPBELL
2/11		METAMUCIL 5 GM. PO TID			CAMPBELL
2/11	2/14	BETHANECHOL CHLORIDE 10 MG. PO TID			STEINBERG
END OF PROFILE 2/17/72					

PROBABLE DRUG-DRUG INTERACTIONS FOR KAREN SMITH

NO. 6572810

LITHIUM EXCRETION IS INCREASED BY AMINOPHYLLINE, SODIUM BICARBONATE AND LARGE DOSES OF SODIUM CHLORIDE. LOW SODIUM INTAKE MAY PRECIPITATE LITHIUM TOXICITY.

MONOAMINE OXIDASE INHIBITORS POTENTIATE THE PHARMACOLOGICAL EFFECTS OF AMPHETAMINES, METHYLPHENIDATE (RITALIN), TRICYCLIC ANTIDEPRESSANTS, HYPOLYCEMICS AND SYMPATHOMIMETICS SUCH AS EPHEDRINE, METARAMINOL (ARAMINE), PHENYLEPHRINE AND PHENYLPROPANOLAMINE. CONCOMITANT USE WITH MEPERIDINE OR LEVODOPA INCREASES INCIDENCE OF ADVERSE EFFECTS.

SULFONAMIDES MAY POTENTIATE THE HYPOGLYCEMIC RESPONSE TO ORAL HYPOLYCEMICS AND ELEVATE SERUM LEVELS OF METHOTREXATE. CONCOMITANT USE WITH METHENAMINE COMPOUNDS FREQUENTLY RESULTS IN CRYSTALLURIA AND THE FORMATION OF A PRECIPITATE.

ANTIHISTAMINES MAY PRODUCE ADDITIVE CNS DEPRESSANT EFFECTS WHEN USED CONCOMITANTLY WITH ETHYL ALCOHOL, BARBITURATES AND PHENOTHIAZINES. THEY MAY POTENTIATE THE PHARMACOLOGICAL ACTIVITY OF ANTICHOLINERGICS AND THE ADVERSE EFFECTS OF TRICYCLIC ANTIDEPRESSANTS.

FOR FURTHER INFORMATION CALL DRUG INFORMATION CENTER EXT 1234

ILLUSTRATION II

Patient Medication Profile. Example II

MODERN HOSPITAL
DEPARTMENT OF PHARMACY
CUMULATIVE MEDICATION PROFILE FOR ROBERT E. JOHNSON

NO. 8363820		ROOM 723	AGE 78
-------------	--	----------	--------

<u>START</u>	<u>STOP</u>	<u>MEDICATION ORDERED</u>	<u>PHYSICIAN</u>
2/02	2/03	DIGOXIN 0.25 MG. PO TID	RILEY
2/02	2/02	BISACODYL 5 MG. PO BID	VINCENT
2/03	2/03	BISACODYL 10 MG. R	VINCENT
2/03	2/03	CASTOR OIL 30 ML. PO	VINCENT
2/03		DIGOXIN 0.25 MG. PO QD	RILEY
2/03	2/03	PENTOBARBITAL SODIUM 100 MG. PO HS	VINCENT
2/04	2/04	DIGOXIN 0.25 MG. IM	VINCENT
2/04	2/04	ATROPINE SULFATE 0.4 MG. IM PRE-OP	VINCENT
2/04	2/04	MEPERIDINE HYDROCHLORIDE 50 MG. IM PRE-OP	VINCENT
2/04	2/04	PROMETHAZINE HYDROCHLORIDE 25 MG. IM PRE-OP	VINCENT
2/04	2/05	MEPERIDINE HYDROCHLORIDE 100 MG. IM Q 4H PRN	RILEY
2/04	2/06	POTASSIUM CHLORIDE 40 MEQ. IV IN D5W 500 ML.	VINCENT
2/04	2/06	MULTIVITAMINS 10 ML. IV IN D5W 1000 ML.	VINCENT
2/05	2/11	METAMUCIL 5 GM. PO BID	RILEY
2/05	2/07	PENICILLIN G POTASSIUM 1,000,000 UNITS IV Q 6H	RILEY
2/05	2/06	MEPERIDINE HYDROCHLORIDE 50 MG. IM Q 4H PRN	VINCENT
2/06	2/08	PENTAZOCINE 30 MG. IM Q 4H PRN	VINCENT
2/07	2/11	AMPICILLIN 0.5 GM. IV Q 6H	RILEY
2/07	2/08	TRIMETHOBENZAMIDE HCL 0.2 GM. R Q 6H PRN	HOLLAND
2/08	2/11	PERCHLORPERAZINE MALEATE 10 MG. IM Q 6H PRN	VINCENT
2/10	2/15	MAALOX 30 ML. PO QID	RILEY
2/11	2/13	CHLORDIAZEPOXIDE HYDROCHLORIDE 10 MG. PO TID	RILEY

CONTINUED ON NEXT PAGE

ROBERT E. JOHNSON		NO. 8363820	ROOM 723	PAGE 2
2/11	2/15	GENTAMICIN SULFATE 40 MG. Q 12H		CUTTS
2/11	2/11	LIDOCAINE HYDROCHLORIDE 2 GM. IN DSW 1000 ML.		CUTTS
2/11	2/11	FUROSEMIDE 40 MG. IV		CUTTS
2/11	2/11	SODIUM BICARBONATE 50 PCT, 150 ML IV		CUTTS
2/11	2/11	MAGNESIUM SULFATE 10 PCT, 10 ML IV		CUTTS
2/11	2/12	HYDROCORTISONE SODIUM SUCCINATE 100 MG. IV Q6H		CUTTS
2/11	2/11	METARAMINCL 10 MG. IV		CUTTS
2/11	2/11	METHYLPREDNISOLONE SOD. SUCCINATE 0.5 GM. IV		CUTTS
2/11	2/11	FUROSEMIDE 200 MG. IV		CUTTS
2/11		POTASSIUM CHLORIDE SYRUP 25 MEQ. PO TID		RILEY
2/11	2/15	FUROSEMIDE 40 MG. PO QD		CUTTS
2/12	2/14	NEOSPORIN GU IRRIGANT		VINCENT
2/12	2/16	CEPHALOTHIN SODIUM 2 GM. IV Q 6H		RILEY
2/13	2/15	HEPARIN SODIUM 1000 UNITS IV Q 6H		VINCENT
2/14	2/15	DIPHENHYDRAMINE HCL 50 MG. PO HS PRN		RILEY
2/16		PHENOBARBITAL 32 MG. PO QID		RILEY
2/16		CHLORAL HYDRATE 0.5 GM. PO HS		RILEY
2/16		WARFARIN SODIUM 10 MG. PO QD		RILEY

END OF PROFILE 2/17/72

PROBABLE DRUG-DRUG INTERACTIONS FOR ROBERT E. JOHNSON

NO. 8363820

DIGITALIS GLYCOSIDES ARE PHARMACOLOGICALLY POTENTIATED BY PARENTERAL CALCIUM PREPARATIONS AND DIURETICS PRODUCING POTASSIUM AND MAGNESIUM DEFICIENCIES. AMPHOTERICIN B (FUNGIZONE) MAY PRODUCE HYPOKALEMIA PRECIPITATING DIGITALIS TOXICITY. SYMPATHOMIMETICS MAY INCREASE INCIDENCE OF CARDIAC ARRHYTHMIAS.

BARBITURATES-ADDITIVE EFFECTS MAY BE SEEN WITH THE CONCOMITANT USE OF ANTIHISTAMINES, PHENOTHIAZINES AND OTHER CNS DEPRESSANTS. THEY MAY BE POTENTIATED BY PROCARBAZINE (MATULANE). THEY MAY DECREASE THERAPEUTIC EFFECTS OF ORAL ANTICOAGULANTS, TRICYCLIC ANTIDEPRESSANTS AND GRISEOFULVIN. THEY MAY VARIABLY EFFECT SERUM DIPHENYLHYDANTICIN LEVELS.

CHLORAL HYDRATE VARIABLY EFFECTS THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS.

ORAL ANTICOAGULANTS ARE POTENTIATED BY ACETAMINOPHEN, ESTROGENS, ANABOLIC STEROIDS, CHLORAMPHENICOL, CHOLESTYRAMINE (QUEMID), CLOFIBRATE (ATROMID S), D-THYROXINE, PHENYLBUTAZONE (BUTAZOLIDIN) AND PHENYRAMIDOL (ANALEXIN). THEY MAY BE POTENTIATED BY AMINOGLYCOSIDE ANTIBIOTICS, DIPHENYLHYDANTICIN, INDOMETHACIN, QUINIDINE AND SALICYLATES. THEY ARE ANTAGONIZED BY ETHYL ALCOHOL, BARBITURATES, ETHCHLORVYNOL, GRISEOFULVIN AND GLUTETHIMIDE. THEY ARE VARIABLY AFFECTED BY CHLORAL HYDRATE.

FOR FURTHER INFORMATION CALL DRUG INFORMATION CENTER EXT 1234

IV. CONCLUSIONS

The design of this computerized drug-drug interaction file offers several unique features.

1. The program reports important drug-drug interactions with each drug entity the patient is receiving. The system is not limited to the reporting of specific interactions which may occur with the patient's current therapeutic regimen.
2. The reporting format is designed to provide practical information in a concise summary which can be easily understood and utilized in any patient care environment.
3. The printout may be incorporated into a patient's medical record or used strictly as a reference source to screen for drug-drug interactions.
4. The file is compatible with existing computerized medication profiles and record systems as well as computerized drug information services.
5. The use of the drug-drug interaction file is not limited to a hospital or a comprehensive ambulatory patient care facility. The system may be incorporated into a computerized drug information service coordinated by a regional drug information network and offered to community practitioners on a subscription basis.

6. The various components of the system can be assembled in a manner which would create a cross-indexed manual of human drug-drug interactions. This aspect of the system would be especially useful to individuals without access to electronic data processing facilities.
7. As an added feature the cumulative patient medication profile can be used as a dispensing record for a medication distribution system.

V. REFERENCES CITED

1. Melmon, K.L.: "Preventable drug reactions - causes and cures," New Eng. J. Med., 248:1361-1368, 1971.
2. Seidl, L.G., et al.: "Studies on the epidemiology of adverse drug reactions. III. Reactions in patients on a general medical service," Bull. Johns Hopkins Hosp., 119:299-315, 1966.
3. Hurwitz, N.: "Admissions to hospital due to drugs," Brit. Med. J., 1:539-540, 1969.
4. Dunphy, T.W.: "The pharmacist's role in the prevention of adverse drug interactions," Am. J. Hosp. Pharm., 26:366, 1969.
5. Slining, J., et al.: "Development of a drug incompatibility file and its use in patient medication profile reviews," Am. J. Hosp. Pharm., 27:459, 1970.
6. Hansten, P.D.: "Retrieval and utilization of drug interaction information," Am. J. Hosp. Pharm., 27:469, 1970.
7. Willig, S.H.: "Legal considerations for the pharmacist undertaking new drug consultation responsibilities," Food Drug Cosmetic Law J., 25:444, 1970.
8. Sjoerdsma, A.: "Catecholamine drug interactions in man," Pharmacol. Rev., 18:673-683, 1966.
9. Hunninghake, D.B., et al.: "Drug interactions with warfarin," Arch. Intern. Med., 121:349-352, 1968.

10. Field, J.B., et al.: "Potentiation of acetohexamide hypoglycemia by phenylbutazone," New Eng. J. Med., 277:889-894, 1967.
11. Blackwell, B. "Hypertensive crisis due to monoamine-oxidase inhibitors," Lancet, 2:849-851, 1963.
12. Lockett, M.F.: "Combining the antidepressant drugs (Letter)," Brit. Med. J., 1:921, 1965.
13. Domino, E.F.: "Barbiturate intoxication in a patient treated with MAOI (Letter)," Am. J. Psychiat., 118:941, 1962.
14. Soeldner, J.S.: "Hypoglycemia in tolbutamide-treated diabetes (Letter)," J. Am. Med. Assoc., 193-398, 1965.
15. Boulos, B.M., et al.: "Hazard of simultaneous administration of phenothiazines and piperazine (Letter)," New Eng. J. Med., 280-1245, 1969.
16. Goodman, L.S. and Gilman, A. (Ed.): "The Pharmacological Basis of Therapeutics," 4th Ed., The MacMillan Company, New York, 1970, pp. 22-25.
17. Hartshorn, E.A.: "Handbook of Drug Interactions," Donald E. Francke, Cincinnati, 1970, pp. 7-11.
18. Jawetz, E.: "The use of combinations of antimicrobial drugs," Ann. Rev. Pharmacol., 8:151, 1968.
19. Mirkin, B.L. and Wright, F.: "Drug interactions: Effect of

methylphenidate on the disposition of diphenylhydantoin in man, " Neurol., 21:1123, 1971.

20. Kupferberg, H.J., et al.: "Effect of methylphenidate on plasma anticonvulsant levels, " Clin. Pharmacol. Therap., 13:201 (March-April) 1972.
21. Schukit, M., et al.: "Tricyclic antidepressant and monoamine oxidase inhibitors, " Arch. Gen. Psychiat., 24:509, 1971.
22. Winston, F.: "Combined antidepressant therapy, " Brit. J. Psychiat., 118:301, 1971.
23. Cucinell, S.A., et al.: "The effect of chloral hydrate on bishydroxycoumarin metabolism, " J. Am. Med. Assoc., 197:366, 1966.
24. Sellers, E.H. and Koch-Weser, J.: "Potentiation of warfarin-induced hypoprothrombinemia by chloral hydrate, " New Eng. J. Med., 282:827, 1970.
25. Griner, P.F., et al.: "Chloral hydrate and warfarin interaction: Clinical significance", Ann. Intern. Med., 74:540, 1971.
26. Bell, J.E.: "Case presentation: Drug Information Center, Mercy Hospital, " Paper presented at the Institute on Drug Interactions and Clinical Communications, Key Biscayne, Florida, (Oct. 19) 1971.

27. Elking, Sister Mary and Kabat, H.F.: "Drug induced modifications of laboratory test values," Am. J. Hosp. Pharm., 25:485, 1968.

APPENDIX I

Source Document

00086 Acetaminophen

Acetaminophen elevates the anticoagulant response to oral anticoagulants. (3, 4)

00124 Acetazolamide

Acetazolamide (Diamox), urinary alkalinizing agent, elevates serum levels of amphetamines (42), tricyclic antidepressants (33, 37) and quinidine (78) by enhancing renal reabsorption. It may antagonize the activity of methenamine compounds. (79)

00167 Alcohol, Ethyl

Ethyl alcohol-additive effects may be seen with CNS depressants (26, 54) and antihistamines (26). It may antagonize the pharmacological effects of the oral anticoagulants (28) and diphenylhydantoin (104). It may enhance the adverse effects of guanethidine (29), nitroglycerin (27), disulfiram (Antabuse) (30), metronidazole (Flagyl) (31) and tricyclic antidepressants (21). It prolongs the action of insulin. (129)

00205 Allopurinol

Allopurinol potentiates the effects of bishydroxycoumarin (10), and mercaptopurine (11, 58). It may increase hepatic

iron concentration. (140)

00299 Antacids

Antacids containing divalent and trivalent cations decrease oral absorption of tetracyclines. Antacids should not be administered simultaneously with enteric coated products. (6)

Sodium polystyrene resin (Kayexalate) binds magnesium and calcium ions found in antacids resulting in systemic alkalosis. (176)

00337 Amantadine

Amantadine (Symmetrel) potentiates the pharmacological effects produced by levodopa. (9)

00434 Aminophyllin

Aminophyllin may impair the therapeutic response to lithium carbonate by increasing the renal excretion of lithium ions. (80)

00515 Aminosalicic Acid

Aminosalicic acid plasma levels are elevated by probenecid (Benemid). (81)

00566 Ammonium chloride

Ammonium chloride (urinary acidifier) may decrease renal reabsorption of amphetamines (42) and tricyclic antidepressants (33, 37).

00604 Amphotericin B

Amphotericin B (Fungizone) may produce hypokalemia

precipitating digitalis toxicity. (82) It may potentiate neuromuscular blockade of skeletal muscle relaxants. (82)

00647 Ampicillin

Ampicillin plasma levels are increased by concomitant use of probenecid (Benemid). (43, 56)

00698 Amphetamines

Amphetamines potentiate MAOI (20) and antagonize the effects of guanethidine (40). Phenothiazines may antagonize the central effects of amphetamines (41). Urine acidifying agents decrease renal reabsorption and urinary alkalinizers such as acetazolamide (Diamox), sodium bicarbonate and thiazide diuretics increase reabsorption. (42)

00744 Angiotensin Amide

Angiotensin amide (Hypertensin)-induced antidiuresis and antinatriuresis is reversed by ethacrynic acid (Edecrin) and furosemide (Lasix). (44)

00752 Anabolic Steroids

Anabolic steroids may potentiate the activity of oral anti-coagulants (63), phenylbutazone (Butazolidin) and oxyphenbutazone (Tandearil) (155, 156) They may decrease insulin requirements in diabetics. (188)

00787 Anticholinergic Drugs

Anticholinergic drugs may potentiate quinidine (83) and the

secondary pharmacological effects of antihistamines and tricyclic antidepressants. Propranolol (Inderal)-induced adverse effects are antagonized by anticholinergics. (84) They may produce extrapyramidal symptoms when used simultaneously with methotrimeprazine (Levoprome). (149)

00825 Anticoagulants, Oral

Oral anticoagulants are potentiated by acetaminophen (3, 4) estrogens (98), anabolic steroids (63), chloramphenicol (64), cholestyramine (Cuemid) (68), clofibrate (Atromid S) (63), Phenylbutazone (Butazolidin) (28, 39) and phenylramidol (Analexin) (72). They may be potentiated by aminoglycoside antibiotics (64), diphenylhydantoin (69), indomethacin (71), quinidine (28, 185) and salicylates (13). They are antagonized by ethyl alcohol (28), barbiturates (49), ethchlorvynol (117), griseofulvin (28, 72) and glutethimide (49, 70). They are variably affected by chloral hydrate (38, 65, 66).

00876 Antidepressants, Tricyclic

Tricyclic antidepressants may potentiate the adverse effects of MAOI (21) and ethyl alcohol (21, 59) and the pharmacological effects of sympathomimetics (36), thyroid preparations (35), antihistamines and anticholinergics. They may antagonize guanethidine (60, 61, 62). Barbiturates appear to decrease therapeutic activity. (38) They are potentiated by

methylphenidate. (34) Urine acidifying agents decrease renal reabsorption and urine alkalinizing agents increase reabsorption. (33, 37)

00884 Antihistamines

Antihistamines may produce additive CNS depressant effects when used concomitantly with ethyl alcohol (26), barbiturates (55) and phenothiazines (157). They may potentiate the pharmacological activity of anticholinergics and the adverse effects of tricyclic antidepressants.

00892 Antihypertensive Agents

Antihypertensive agents may be potentiated by methotrimeprazine (Levoprome) (149), procainamide (Pronestyl) (125, 168) and propranolol (Inderal) (84, 126).

00914 Ascorbic Acid

Ascorbic acid (urinary acidifier) may antagonize amphetamines (42) and tricyclic antidepressants (33, 37).

00957 Barbiturates

Barbiturates-additive effects may be seen with the concomitant use of antihistamines, phenothiazines and other CNS depressants. (55) They may be potentiated by procarbazine (Matulane) (48). They may decrease therapeutic effects of oral anticoagulants (49), tricyclic antidepressants (38) and griseofulvin (37).

They may variably effect serum diphenylhydantoin levels.

(45, 46)

01058 Bishydroxycoumarin

Bishydroxycoumarin may potentiate the sulfonylureas and increase serum levels of diphenylhydantoin (50). It is potentiated by acetaminophen (3, 4), estrogens (98), anabolic steroids (63), chloramphenicol (64), cholestyramine (Cuemid) (68), clofibrate (Atromid S) (63), d-thyroxine (63), phenylbutazone (Butazolidin) (28, 39) and phenylramidol (Analexin) (72). It may be potentiated by aminoglycoside antibiotics (64), diphenylhydantoin (69), indomethacin (71) and salicylates (13). It is antagonized by ethyl alcohol (28), barbiturates (49), ethchlorvynol (117), griseofulvin (28, 73) and glutethimide (49, 70). It is variably affected by chloral hydrate. (38, 65, 66)

01090 Bisacodyl

Bisacodyl (Dulcolax) tablets should not be taken concomitantly with antacids. (182)

01139 Calcium Preparations (Parenteral)

Calcium ions administered parenterally may pharmacologically potentiate digitalis glycosides. (74, 75)

01147 Carbenicillin

Carbenicillin (Pyopen, Geopen) plasma levels may be elevated and prolonged by probenecid (Benemid) (186, 187)

01171 Cephalosporins

Cephalosporins, all-plasma levels are elevated by probenecid (Benemid) (43, 76). Concomitant administration of colistin increases incidence of nephrotoxicity. (96)

01236 Chloral Betaine

Chloral betaine (Beta-Chlor) variably effects the anticoagulant response to oral anticoagulants. (38, 65, 66)

01317 Chloral Hydrate

Chloral hydrate variably effects the anticoagulant response to oral anticoagulants. (38, 65, 66)

01368 Chloramphenicol

Chloramphenicol may potentiate oral anticoagulants (64), diphenylhydantoin (67) and sulfonylureas (67).

01406 Diuretics

Diuretics producing potassium and magnesium deficiencies may precipitate digitalis toxicity (94, 95). Concomitant use with corticosteroids may result in excessive potassium loss (102). Diuretics may antagonize the activity of oral hypoglycemics. (115, 163, 164)

01449 Cholestyramine

Cholestyramine (Cuemid) may elevate the anticoagulant response to oral anticoagulants. (68) It decreases absorption of thyroid preparations by binding thyroxine and triiodo-

thyronnine. (177)

01481 Clofibrate

Clofibrate (Atromid S) pharmacologically elevates the anticoagulant response to oral anticoagulants (63). It may inhibit platelet adhesiveness. (179)

01546 Colistin

Colistin (Coly-Mycin) enhances neuromuscular blockade of skeletal muscle relaxants. (97) Concomitant administration of parenteral cephalosporins increases incidence of nephrotoxicity. (96)

01589 Corticosteroids

Corticosteroids may be potentiated by estrogens. (99) They may pharmacologically antagonize hypoglycemics (77, 115) and decrease salicylate plasma levels (15). Diphenylhydantoin may decrease therapeutic response to corticosteroids. (100, 101) Concomitant use with diuretics may result in excessive potassium loss. (102)

01627 Corticotropin

Corticotropin (ACTH) may be potentiated by estrogens (99). It may pharmacologically antagonize hypoglycemics (77, 115) and decrease salicylate plasma levels (15). Diphenylhydantoin may decrease response to corticosteroids. (100, 101) Concomitant use with diuretics may result in excessive potassium loss. (102)

01678 Dapsone

Dapsone (Avlosulfon) plasma levels are increased by probenecid (Benemid). (103)

01759 Digitalis Glycosides

Digitalis glycosides are pharmacologically potentiated by parenteral calcium preparations (74, 75) and diuretics producing potassium and magnesium deficiencies (94, 95). Amphotericin B (Fungizone) may produce hypokalemia precipitating digitalis toxicity. (82) Sympathomimetics may increase incidence of cardiac arrhythmias. (94)

01791 Diphenylhydantoin

Diphenylhydantoin is potentiated by chloramphenicol (67), disulfiram (Antabuse) (105) and isoniazid (106, 107). It may be antagonized by ethyl alcohol (104) and phenylramidol (Analexin) (109). It may potentiate oral anticoagulants (69) and methotrexate (108). It may decrease the therapeutic response to corticosteroids. (100, 101)

01848 Dipyridamole

Dipyridamole (Persantine) may potentiate the anticoagulant activity of heparin. (110, 178)

01880 Disulfiram

Disulfiram (Antabuse) potentiates diphenylhydantoin. (105) Concomitant use with isoniazid (111), ethyl alcohol (30) and

metronidazole (Flagyl) (112, 113) enhances the incidence of adverse effects.

01929 Echothiophate Iodide

Echothiophate iodide (Phospholine iodide) potentiates the pharmacological effects of succinylcholine. (114)

01961 Ephedrine

Ephedrine potentiates hypertensive reactions with MAOI. (23) It antagonizes the adrenergic neuron blockade produced by guanethidine (Ismelin). (40)

02011 Epinephrine

Epinephrine, and to a lesser extent, other adrenergic agents may decrease activity of hypoglycemic agents. (115)

02062 Estrogens

Estrogens pharmacologically elevate the anticoagulant activity of oral anticoagulants. (98) They may potentiate corticosteroid activity. (99)

02100 Ethacrynic Acid

Ethacrynic acid potentiates ototoxicity of aminoglycoside antibiotics. (116) It may produce potassium and magnesium deficiencies precipitating digitalis toxicity. (94, 95) Concomitant use with corticosteroids may enhance potassium loss. (102) It may antagonize the activity of oral hypoglycemics. (163, 164)

02143 Ethchlorvynol

Ethchlorvynol (Placidyl) antagonizes the anticoagulant activity of oral anticoagulants. (117)

02194 Folic Acid

Folic acid antagonizes the antineoplastic activity of methotrexate. (118)

02232 Furosemide

Furosemide may produce potassium and magnesium deficiencies precipitating digitalis toxicity. (94, 95) Concomitant use with corticosteroids may enhance potassium loss. (102) It enhances the effects of tubocurarine. (119) It may antagonize the activity of oral hypoglycemics. (163, 164)

02275 Gentamicin

Gentamicin in combination with other aminoglycoside antibiotics increases incidence of ototoxicity and nephrotoxicity. (120) Ethacrynic acid potentiates the ototoxicity. (116) It enhances the blockade of skeletal muscle relaxants. (97)

02313 Glutethimide

Glutethimide (Doriden) decreases anticoagulant response to oral anticoagulants. (49, 70)

02364 Glyceryl Guaiacolate

Glyceryl guaiacolate may potentiate the anticoagulant

activity of heparin. (110, 118)

02402 Griseofulvin

Griseofulvin may decrease the anticoagulant activity of oral anticoagulants. (28, 73) It is antagonized by barbiturates which may impair absorption. (37)

02445 Guanethidine

Guanethidine may be potentiated by procainamide (125), propranolol (126) and quinidine (127). It is antagonized by amphetamines (40), tricyclic antidepressants (60, 61, 62), ephedrine (40) and methylphenidate (40, 122, 123). It may potentiate phenylephrine (124) and decrease activity of hypoglycemics (88, 89). Ethyl alcohol (29), methotrimeprazine (Levoprome) (121), procarbazine (Matulane) (48) and thiazide diuretics (32) may potentiate orthostatic hypotension.

02496 Heparin

Heparin induced anticoagulant activity may be enhanced by dipyridamole (Persantine) (110) and glyceryl guaiacolate (110, 118).

02542 Hypoglycemic Agents, Oral

Oral hypoglycemic agents may be potentiated by chloramphenicol (67). MAOI (22), phenylbutazone (Butazolidin) (2, 165), propranolol (Inderal) (166, 169), bishydroxycoumarin (162),

phenylramidol (Analexin) (162) and salicylates (17). The hypoglycemic effects are antagonized by corticosteroids (77), diuretics (115, 163, 164) and guanethidine (Ismelin) (88, 89).

02585 Indomethacin

Indomethacin may pharmacologically elevate the activity of oral anticoagulants. (71) Indomethacin plasma levels may be increased by probenecid (Benemid) (128) and decreased by salicylates (53).

02623 Insulin

Insulin may be pharmacologically antagonized by guanethidine. (88, 89) Ethyl alcohol may prolong the action of insulin. (129) Glucocorticoids, thyroid, epinephrine and thiazide diuretics may increase insulin requirements. (115)

02674 Iron Salts

Iron salts should not be used simultaneously with allopurinol (Zyloprim). (140) Antacids may decrease iron absorption. (141) Iron salts may impair the absorption of oral tetracyclines. (183)

02712 Isoniazid

Isoniazid increases plasma levels of diphenylhydantoin. (106, 107) It may be antagonized by ethyl alcohol. (130) Concomitant use with disulfiram (Antabuse) (111) and meperidine (131) enhances incidence of adverse effects.

01716 D-Thyroxine

D-Thyroxine elevates the anticoagulant response to oral anticoagulants. (63)

02755 Isoproterenol

Isoproterenol is pharmacologically antagonized by propranolol (Inderal). (132)

02801 Kanamycin

Kanamycin in combination with other aminoglycoside antibiotics increases incidence of ototoxicity and nephrotoxicity. (120) Concomitant use with ethacrynic acid potentiates the ototoxicity. (116) It potentiates neuromuscular blockade of skeletal muscle relaxants. (97) When administered by the oral route it may increase the activity of oral anticoagulants. (64)

02852 Kaolin-Pectin

Kaolin-pectin mixtures inhibit the absorption of orally administered lincomycin (Lincocin), (133)

02895 Levodopa

Levodopa may be antagonized by methyldopa (137), pyridoxine (138, 139), reserpine (137) and phenothiazines (85). Concomitant use with MAOI may produce hypertension (136). Additive therapeutic effects may occur with amantadine (Symmetrel). (9)

02933 Lithium Carbonate

Lithium excretion is increased by aminophylline (134), sodium bicarbonate (134) and large doses of sodium chloride (135). Low sodium intake may precipitate lithium toxicity. (135)

02984 Magnesium Salts

Magnesium ions administered parenterally potentiate the neuromuscular blockade of skeletal muscle relaxants. (142)

03034 Meperidine

Meperidine should not be used simultaneously with isoniazid (131) and MAOI (25) - it enhances incidence of adverse effects. It is potentiated by other CNS depressants.

03077 Meprobamate

Meprobamate (Equanil, Miltown) is potentiated by ethyl alcohol. (180, 181)

03115 Mercaptopurine

Mercaptopurine (Purinethol) is potentiated by allopurinol (Zyloprim). (11, 58)

03166 Metaraminol

Metaraminol (Aramine) is pharmacologically potentiated by MAOI. (23)

03204 Methenamine Compounds

Methenamine compounds exhibit optimum activity in a

urine ph of 5.5 or lower. Urine acidifying agents are useful adjuncts while urine alkalinizers decrease activity.

(143) Concomitant use with sulfonamides frequently results in crystalluria and the formation of a precipitate. (143, 144 145)

03247 Methoxyflurane

Methotrexate serum levels are elevated by diphenylhydantoin (108), salicylates (16, 146, 147) and sulfonamides (16, 146, 147). It may impair the immunological response to smallpox vaccine, resulting in vaccina. (148)

03298 Methotrimeprazine

Methotrimeprazine (Levoprome) potentiates the effects of antihypertensive agents (149), other CNS depressants (149) and skeletal muscle relaxants (149). It will produce extrapyramidal symptoms when used simultaneously with anticholinergics. (149)

03361 Methoxyflurane

Methoxyflurane anesthesia in conjunction with tetracycline therapy increases incidence of nephrotoxic effects. (93)

03344 Methyldopa

Methyldopa may antagonize the therapeutic effects of levodopa (137). Additive hypotensive effects may occur with propranolol (Inderal) (84, 150), procainamide (Pronestyl)

(125, 168), methotrimeprazine (Levoprome) (149) and thiazide diuretics (184).

03387 Methlyphenidate

Methylphenidate (Ritalin) potentiates tricyclic antidepressants. (34) It may be potentiated by MAOI. (20, 151) It antagonizes the pharmacological effects of guanethidine (Ismelin). (40, 122, 123)

03425 Metronidazole

Metronidazole (Flagyl) should not be used simultaneously with disulfiram (Antabuse) (112, 113) or ethyl alcohol (31) due to the increased incidence of adverse effects.

03476 Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors potentiate the pharmacological effects of amphetamines (20), methylphenidate (Ritalin) (20, 151), tricyclic antidepressants (21), hypoglycemics (22) and sympathomimetics such as ephedrine (23), metaraminol (Aramine) (24), phenylephrine and phenylpropanolamine. Concomitant use with meperidine (25) or levodopa (136) increases incidence of adverse effects.

03514 Nafcillin

Nafcillin (Unipen) plasma levels are increased by concomitant use of probenecid (Benemid). (154)

03557 Neomycin

Neomycin in combination with other aminoglycoside antibiotics

increases incidence of ototoxicity and nephrotoxicity. (120)

Concomitant use with ethacrynic acid potentiates the ototoxicity.

(116) It potentiates neuromuscular blockade of skeletal muscle relaxants. (97) When administered by the oral route it may increase the activity of oral anticoagulants. (64)

03603 Nitroglycerin

Nitroglycerin may produce hypotension following combined use with ethyl alcohol. (27) Chronic administration of pentaerythritol tetranitrate (Peritrate) may produce a tolerance to nitroglycerin. (152, 153)

03697 Orphenadrine

Orphenadrine (Norflex) in combination with propoxyphene (Darvon) may produce mental confusion and anxiety. (169, 170)

03735 Oxyphenbutazone

Oxyphenbutazone (Tandearil) elevates the anticoagulant response to oral anticoagulants. (28, 39) Oxyphenbutazone plasma levels may be elevated by anabolic steroids. (155, 156)

03743 Penicillin G and Derivatives

Penicillin G and derivatives-plasma levels are elevated by probenecid (Benemid) (8, 43) and salicylates (14).

03751 Pentaerythritol Tetranitrate

Pentaerythritol tetranitrate (Peritrate) therapy may produce a tolerance to nitroglycerin. (152, 153)

03786 Phenothiazines

Phenothiazines may antagonize levodopa (85) and the central effects of amphetamines (41). Additive effects occur with concomitant use of other CNS depressants (161) and antihistamines (157). Additive cardiac depressant effects are possible with quinine. (158, 159, 160) Procarbazine (Matulane) may potentiate the CNS depressant effects of phenothiazines. (48)

03824 Phenylbutazone

Phenylbutazone (Butazolidin) elevates the anticoagulant response to oral anticoagulants (28, 39) and potentiates the hypoglycemic response to sulfonylureas (2, 165). Phenylbutazone plasma levels may be elevated by anabolic steroids. (155, 156)

03867 Phenylephrine

Phenylephrine administered nasally or systemically may be potentiated by guanethidine (Ismelin) (124) and MAOI (23).

03905 Phenylpropanolamine

Phenylpropanolamine may be potentiated by MAOI. (23)

03956 Phenylramidol

Phenylramidol (Analexin) elevates the anticoagulant response to oral anticoagulants (72) and potentiates the activity of diphenylhydantoin (109) and sulfonylureas (162).

03999 Polymyxin B

Polymyxin B (Aerosporin) enhances neuromuscular blockade of skeletal muscle relaxants. (97) In combination with other

aminoglycoside antibiotics it increases incidence of ototoxicity and nephrotoxicity. (120)

04230 Probenecid

Probenecid (Benemid) elevates plasma levels of aminosalicyclic acid (81), dapsone (Avlosulfon) (103), cephalosporins (43, 77), penicillin G and derivatives (8, 43) and indomethacin (128). Salicylates inhibit uricosuric activity of probenecid. (19)

04073 Procainamide

Procainamide (Pronestyl) - additive hypotensive effects may occur with concomitant use of antihypertensive agents. (125, 168)

04138 Procarbazine

Procarbazine (Matulane) may potentiate the effects of phenothiazines and CNS depressants. (48) It may produce additive hypotensive effects with guanethidine (Ismelin). (48)

04170 Propoxyphene

Propoxyphene (Darvon) in combination with orphenadrine (Norflex) may produce mental confusion and anxiety. (169, 170)

04219 Propranolol

Propranolol (Inderal) may potentiate oral hypoglycemics (166, 167) and antihypertensives (84, 126). It antagonizes pharmacological actions of sympathomimetics. (132) Propranolol-induced adverse effects are antagonized by anticholinergics. (84) Additive cardiac depressant effects are possible with quinidine (171,

172) and phenothiazines (158, 159, 160)

04251 Pyridoxine

Pyridoxine (Vitamin B6) antagonizes the pharmacological effects of levodopa. (138, 139)

04308 Quinidine

Quinidine may potentiate guanethidine (127), oral anticoagulants (28, 185) and the neuromuscular blockade of muscle relaxants (173). It may be potentiated by anticholinergics (83). Acetazolamide (Diamox), sodium bicarbonate and thiazide diuretics increase renal reabsorption (5, 78, 175). Additive cardiac depressant effects are possible with propranolol (171, 172) and phenothiazines (158, 159, 160).

04340 Reserpine

Reserpine is potentiated by methotrimeprazine (Levoprome). (149) It may antagonize the effects of levodopa. (137)

04383 Salicylates

Salicylates elevate the anticoagulant response to oral anticoagulants (13), increase plasma levels of unbound penicillin G and derivatives (14) and potentiate methotrexate (16) and sulfonylureas (17). Salicylate plasma levels may be decreased by corticosteroids. (15) They may decrease serum levels of indomethacin (Indocin) (53) and inhibit uricosuric activity of sulfinpyrazone (Anturane) (18) and probenecid (Benemid) (19).

04421 Skeletal Muscle Relaxants

Surgical skeletal muscle relaxants are potentiated by aminoglycoside antibiotics (97), amphotericin B (82), furosemide (119), magnesium ions (142), methotrimeprazine (Levoprome) (149), quinine (173) and thiazide diuretics (174). Echothiophate iodide potentiates the effects of succinylcholine. (114)

04472 Small Pox Vaccine

Small pox vaccination may result in generalized vaccina with concomitant use of methotrexate. (148)

04510 Sodium Bicarbonate

Sodium bicarbonate elevates serum levels of amphetamines (42), tricyclic antidepressants (33, 37) and quinidine (5, 78, 175) by enhancing renal reabsorption. It may antagonize methenamine compounds (143) and lithium carbonate (134) and decrease oral absorption of tetracyclines (91).

04553 Sodium Chloride

Sodium chloride in large doses may antagonize pharmacological effects of lithium carbonate. (135) Low sodium intake may precipitate lithium toxicity. (135)

04618 Sodium Polystyrene Sulfonate

Sodium polystyrene sulfonate resin (Kayexalate) binds magnesium and calcium ions found in antacids resulting in systemic alkalosis. (176)

04650 Streptomycin

Streptomycin in combination with aminoglycoside antibiotics increases incidence of ototoxicity and nephrotoxicity. (120)

Ethacrynic acid potentiates the ototoxicity. (116) It potentiates neuromuscular blockade of skeletal muscle relaxants. (97)

04693 Sulfinpyrazone

Sulfinpyrazone (Anturane) induced uricosuria is inhibited by salicylates. (18)

04731 Sulfonamides

Sulfonamides may potentiate the hypoglycemic response to oral hypoglycemics (1) and elevate serum levels of methotrexate (16, 146, 147). Concomitant use with methenamine compounds frequently results in crystalluria and the formation of a precipitate. (143, 144, 145)

04782 Tetracyclines

Tetracycline absorption is decreased by antacids (90) containing divalent or trivalent cations, sodium bicarbonate (91) and iron salts (183). It may elevate anticoagulant response to oral anticoagulants (92) and potentiate nephrotoxic effects of methoxyflurane (Penthrane) (93).

04820 Thiazide Diuretics

Thiazide diuretics may precipitate digitalis toxicity (94, 95) and antagonize the effects of hypoglycemics (115, 163, 164). Neuro-

muscular blockade produced by surgical muscle relaxants may be enhanced. (174) Concomitant use with corticosteroids may result in excessive potassium loss. (162) They may produce additive hypotensive effects with guanethidine (Ismelin) (32) and methyldopa (Aldomet) (184).

04863 Thyroid Preparations

Thyroid preparations may potentiate the anticoagulant response to oral anticoagulants. (63) Cholestyramine decreases absorption by binding thyroxine and triiodothyronine. (177) They may decrease activity of hypoglycemic agents. (115)

APPENDIX II

Alphabetical Cross-Index

A

Acenocoumarol	00825
Acetaminophen	00086
Acetazolamide	00124
Acetohexamide	02542
Acetophenazine	
Maleate	03786
Acetyldigitoxin	01759
Aldactazide	04820
Adiphenine HCl	00787
Allopurinol	00205
Alphaprodine	00256
Alverine Citrate	00787
Amantadine	00337
Aminophyllin	00434
Aminosalicyclic Acid	00515
Amitriptyline HCl	00876
Ammonium Chloride	00566
Amobarbital	00957
Amphetamine	
Sulfate	00698
Amphotericin B	00604
Ampicillin	00647
Angiotensin Amide	00744
Antacids	00299
APC	04383
Aprobarbital	00957
Ascorbic Acid	00914
Aspirin	04383
Atropine Sulfate	00787
Azapetine HCl	00892
Azo-Gantanol	04731
Azo-Gantrisin	04731

B

Barbital	00957
Barbital Sodium	00957
Bendroflumethiazide	04820

Benzestrol	02062
Benzthiazide	04820
Bethamethasone	01589
Biperiden	00787
Biphetamine-T	00698
Bisacodyl	01090
Bishydroxycoumarin	01058
Butabarbital Sodium	00957
Butalbital	00957
Butaperazine	
Maleate	03786
Butazolidin Alka	03824

C

Calcium Chloride,	
Injection	01139
Calcium Gluconate,	
Injection	01139
Carbenicillin	01147
Carbrital	00957
Carphenazine	
Maleate	03786
Cholestyramine	01449
Chloral Betaine	01236
Chloral Hydrate	01317
Chloramphenicol	01368
Chlormerodrin	01406
Chlorothiazide	04820
Chlorotrianisene	02062
Chlorpromazine	
HCl	03786
Chlorpropamide	02542
Chlortetracycline	04782
Chlorthalidone	01406
Clofibrate	01481
Colistin	01546
Combidi	03786

Corticotropin	01627	Doxycycline	04782
Cortisone	01589	D-Thyroxine	01716
C-Quens	02062	Dyazide	04820
Cyclothiazide	04820		
Cycrimine HCl	00787	<u>E</u>	
Cyproheptadine HCl	00884		
<u>D</u>		Echothiophate Iodide	01929
Dapsone	01678	Empirin	04383
Darvon Compound	04170	Ephedrine	01961
	04383	Epinephrine	02011
Darvon Compound-65	04170	Eskatrol	00167
	04383		03786
Decamethonium		Estradiol	02062
Bromide	04421	Estradiol Benzoate	02062
Demethylchlor-		Estradiol Dipropio-	
tetracycline	04782	nate	02062
Desbutal	00698	Estrone	02062
	00957	Equagesic	03077
Desipramine HCl	00876		04383
Deslanoside	01759	Ethacrynic Acid	02100
Dexamethasone	01589	Ethchlorvynol	02143
Dexamyl	00698	Ethinyl Estradiol	02062
	00957	Ethyl Alcohol	00167
Dextroamphetamine		Ethyl Biscoumacetate	00825
Sulfate	00698	Ethylestrenol	00752
Dibutoline Sulfate	00787	<u>F</u>	
Dienestrol	02062		
Diethylstilbestrol	02062	Ferrous Fumarate	02674
Diethylstilbestrol		Ferrous Gluconate	02674
Diphosphate	02062	Ferrous Sulfate	02674
Digitalis	01759	Fludrocortisone	01589
Digitalis Glycosides	01759	Fluphenazine Enan-	
Digitoxin	01759	thate	03786
Digoxin	01759	Fluphenazine HCL	03786
Dimethyl Tubocura-		Fluprednisolone	01589
rine Iodide	04421	Folic Acid	02194
Diphenhydramine		Furosemide	02232
Hydrochloride	00884	<u>G</u>	
Diphenylhydantoin	01791		
Dipyridamole	01848	Gentamicin	02275
Disulfiram	01880	Glutethimide	02313
Diupres	04340	Glyceryl Guaicolate	02364
	04820	Griseofulvin	02402
Doxepin HCL	00876	Guanethidine	02445

H

Heparin	02496
Hetacillin	00647
Hexafluorenum	
Bromide	04421
Hexobarbital	00957
Hydrochlorothiazide	04820
Hydrocortisone	01589
Hydroflumethiazide	04820
Hydropres	04340

I

Imipramine	00876
Indomethacin	02585
Insulin	02633
Isocarboxazid	03476
Isoniazid	02712
Isoproterenol	

K

Kanamycin Sulfate	02801
Kaolin-Pectin	02852

L

Lanatoside C	01757
Levodopa	02895
Levothyroxine	04863
L-Hyoscyamine Sulfate	00787
Liothyronine	04863
Liotrix	04863
Lithium Carbonate	02933

M

Magnesium Sulfate,	
Injection	02984
Meperidine HCL	03034
Mephobarbital	00957
Meproamate	03077
Meralluride	01406
Mercaptomerin Sodium	01406
Mercaptopurine	03115

Mercurophylline	01406
Merethoxylline	01406
Metaraminol	03166
Methacycline	04782
Methallenestril	02062
Methamphetamine HCL	00698
Methandriol	00752
Methandrostenolone	00752
Methdilazine HCL	00884
Methenamine Hippur-	
ate	03204
Methenamine Man-	
delate	03204
Methenamine Sul-	
fosalicylate	03204
Methotrexate	03247
Methotrimoprazine	03298
Methoxyflurane	03361
Methyclorthiazide	04820
Methylatropine Nitrate	00787
Methyldopa	03344
Methylphenidate	03387
Methylprednisolone	01589
Metronidazole	03425

N

Nafcillin	03514
Naldecon	03905
Nandrolone Decanoate	00752
Nandrolone Phen-	
propionate	00752
Neomycin	03557
Nialamide	03476
Nitroglycerin	03603
Norethandrolone	00752
Norgesic	03697
	04383
Nortriptyline HCL	00876

O

Orphenadrine	03697
Ortho-Novum	02062

Ovral	02062	Propranolol	04219
Ovulen	02062	Protriptyline HCL	00876
Oxymetholone	00752	Pyridoxine	04251
Oxyphenbutazone	03735		
Oxytetracycline	04782	<u>Q</u>	
<u>P</u>		Quabain	01759
Paramethasone	01589	Quinethazone	01406
Penicillin G	03743	Quinidine	04308
Pentaerythritol		<u>R</u>	
Tetranitrate	03751	Reserpine	04340
Pentobarbital Sodium	00957		
Perphenazine	03786	<u>S</u>	
Phenelzine	03476	Salicylamide	04383
Phenformin	02542	Scopolamine HBr	00787
Phenindione	00825	Secobarbital	00957
Phenobarbital	00957	Ser-Ap-Es	04340
Phenoxybenzamine			04820
Hydrochloride	00892	Small Pox Vaccine	04472
Phenoxyethyl		Sodium Bicarbonate	04510
Penicillin	03743	Sodium Chloride	04553
Phenylbutazone	03824	Sodium Polystyrene	
Phenprocoumon	00825	Sulfonate Resin	04618
Phenylephrine	03867	Sodium Salicylate	04383
Phenylpropanolamine	03905	Stanozolol	00752
Phenylramidol	03956	Streptomycin	04660
Piperactazine	03786	Succinylcholine	
Piperidolate	00787	Chloride	04421
Polyestradiol Phosphate	02062	Sulfachlorpyridazine	04731
Polymyxin B	03999	Sulfadiazine	04731
Polythiazide	04820	Sulfadimethoxine	04731
Prednisone	01589	Sulfaethidole	04731
Prednisolone	01589	Sulfamerazine	04731
Probenecid	04030	Sulfameter	04731
Procainamide	04073	Sulfamethizole	04731
Procaine Penicillin	03743	Sulfamethoxazole	04731
Procarbazine	04138	Sulfamethoxy-pyri-	
Prochlorperazine	03786	dazine	04731
Procyclidine HCL	00787	Sulfapyridine	04731
Promazine	03786	Sulfinpyrazone	04693
Promethazine HCL	03786	Sulfisoxazole	04731
Promethestrol			
Dipropionate	02062		
Propoxyphene HCL	04170		
Propoxyphene Napsylate	04170		

T

Tetracycline	04782
Thiopropazate	
Dihydrochloride	03786
Thioridazine HCL	03786
Thyroglobulin	04863
Thyroid	04863
Tolazoline HCL	00892
Tolbutamide	02524
Tolinase	02542
Tranylcypromine	03476
Triamcinolone	01589
Triamterene	01406
Trichlormethiazide	04820
Trifluoperazine HCL	03786
Triflupromazine	03786
Trihexyphenidyl	00787
Trimeprazine	00884
Trimethaphen Cam-	
sylate	00892
Tripelennamine	00884
Tubocurarine Chloride	04421

W

Warfarin Sodium	00825
-----------------	-------

APPENDIX III

Message Code Index

<u>Message Code</u>	<u>Drug</u>	<u>Message Code</u>	<u>Drug</u>
00086	Acetaminophen	00744	Angiotensin
00124	Acetazolamide	00752	Ethylestrenol
00167	Ethyl Alcohol		Methandriol
00205	Allopurinol		Methandrostenolone
00256	Alphaprodine		Nandrolone
00299	Antacids		Decanoate
00337	Amantadine		Nandrolone Phenpropionate
00434	Aminophyllin		Norethandrolone
00515	Aminosalicylic Acid		Oxymetholone
00566	Ammonium Chloride		Stanozolol
00604	Amphotericin B	00787	Adiphenine HCL
00647	Ampicillin		Alverine Citrate
	Hetacillin		Atropine Sulfate
00698	Amphetamine Sulfate		Biperiden
	Biphetamine-T		Cycrimine HCL
	Desbutal		Dibutoline Sulfate
	Dexamyl		1-Hyoscyamine Sulfate
	Dextroamphetamine Sulfate		Methylatropine Nitrate
	Eskatrol		Piperidolate
	Methamphetamine HCL		Scopolamine HBr
		00825	Trihexyphenidyl
			Procyclidine HCL
			Acenocoumarol
			Ethyl Biscoumate
			Phenindione
			Phenprocoumon
			Warfarin Sodium

<u>Message Code</u>	<u>Drug</u>	<u>Message Code</u>	<u>Drug</u>
00876	Amitriptyline HCL Desipramine HCL Doxepin HCL Imipramine Nortriptyline HCL Protriptyline HCL	01090 01139	Bisacodyl Calcium Chloride, Injection Calcium Gluconate, Injection
00884	Cyproheptadine Hydro- chloride Diphenhydramine Hydrochloride Methdilazine Hydro- chloride Trimeprazine Tripelennamine	01147 01236 01317 01368 01406	Carbenicillin Chloral Betaine Chloral Hydrate Chloramphenicol Chlormerodrin Chlorthalidone Meralluride Merethoxylline Mercaptomerin Sodium Mercurophylline Quinethazone Triamterene
00892	Azapetine Hydrochloride Phenoxybenzamine Hydrochloride Tolazoline Hydrochloride Trimethaphen Camsylate		
00914	Ascorbic Acid	01449	Cholestyramine
00957	Amobarbital Aprobarbital Barbital Barbital Sodium Butabarbital Sodium Butalbital Carbital Desbutal Dexamyl Hexobarbital Mephobarbital Pentobarbital Sodium Phenobarbital Secobarbital	01481 01546 01589	Clofibrate Colistin Betamethasone Cortisone Dexamethasone Fludrocortisone Fluprednisolone Hydrocortisone Methylprednisolone Paramethasone Prednisolone Prednisone Triamcinolone
01058	Bishydroxycoumarin		

<u>Message Code</u>	<u>Drug</u>	<u>Message Code</u>	<u>Drug</u>
01627	Corticotropin		Ovral
			Ovulen
01678	Dapsone		Polyestradiol Phosphate
01716	D-Thyroxine		Promethestrol Dipropionate
01759	Acetyldigitoxin		
	Deslanoside	02100	Ethacrynic Acid
	Digitalis		
	Digitalis Glycosides	02143	Ethchlorvynol
	Digitoxin		
	Digoxin	02194	Folic Acid
	Lanatoside C		
	Quabain	02232	Furosemide
01791	Diphenylhydantoin	02275	Gentamicin
01848	Dipyridamole	02313	Glutethimide
01880	Disulfiram	02364	Glyceryl Guaiaco- late
01929	Echothiophate Iodide	02402	Griseofulvin
01961	Ephedrine	02445	Guanethidine
02011	Epinephrine	02496	Heparin
02062	Benzestrol	02542	Acetohexamide
	C-Quens		Chlorpropamide
	Chlorotrianisene		Tolbutamide
	Dienestrol		Tolinase
	Diethylstilbestrol		Phenformin
	Diethylstilbestrol Diphosphate	02585	Indomethacin
	Estradiol		
	Estradiol Benzoate	02633	Insulin
	Estradiol Dipropionate	02674	Ferrous Fumarate
	Estrone		Ferrous Gluconate
	Ethinyl Estradiol		Ferrous Sulfate
	Methallenestril		
	Ortho-Novum	02712	Isoniazid

<u>Message Code</u>	<u>Drug</u>	<u>Message Code</u>	<u>Drug</u>
02755	Isoproterenol		Phenelzine Sulfate
02801	Kanamycin		Tranlylcypromine
02852	Kaolin-Pectin	03514	Nafcillin Sodium
02895	Levodopa	03557	Neomycin Sulfate
02933	Lithium Carbonate	03603	Nitroglycerin
02984	Magnesium Sulfate, Injection	03697	Norgesic Orphenadrine
03034	Meperidine	03735	Oxyphenbutazone
03077	Equagesic Meproamate	03743	Penicillin G Phenoxymethyl Penicillin
03115	Mercaptopurine		Procaine Penicillin
03166	Metaraminol	03751	Pentaerythritol Tetranitrate
03204	Methenamine Hippurate Methenamine Mandelate Methenamine Sulfosalicylate	03786	Acetophenazine Maleate Butaperazine Maleate Carphenazine Maleate Chlorpromazine HCL Combid Eskatrol Fluphenazine Enanthate Fluphenazine HCL Perphenazine Piperactazine Prochlorperazine HCL Promazine HCL
03247	Methotrexate		
03298	Methotrimeprazine		
03344	Methyldopa		
03361	Methoxyflurane		
03387	Methylphenidate		
03425	Metronidazole		
03476	Isocarboxazid Nialamide		

<u>Message Code</u>	<u>Drug</u>	<u>Message Code</u>	<u>Drug</u>
	Promethazine HCL	04383	APC
	Thiopropazate		Aspirin
	Dihydrochloride		Empirin
	Thioridazine HCL		Equagesic
	Trifluoperazine		Norgesic
	HCL		Salicylamide
	Triflupromazine		Sodium Salicylate
03824	Butazolidin Alka	04421	Dimethyl Tubo-
	Phenylbutazone		curarine Iodide
03867	Phenylephrine		Decamethonium
			Bromide
03905	Naldecon		Succinylcholine
	Phenylpropanolamine		Chloride
03956	Phenylramidol		Tubocurarine
			Chloride
03999	Polymyxin B	04472	Small Pox
			Vaccine
04030	Probenecid	04510	Sodium Bicar-
			bonate
04073	Procainamide	04553	Sodium Chloride
04138	Procarbazine	04618	Sodium Polysty-
04170	Darvon Compound		rene Sulfonate
	Darvon Compound-65		Resin
	Propoxyphene HCL	04660	Streptomycin
	Propoxyphene		
	Napsylate	04693	Sulfinpyrazone
04219	Propranolol	04731	Azo-Gantrisin
04251	Pyridoxine		Azo-Gantanol
04308	Quinidine		Sulfadiazine
04340	Diupres		Sulfaethidole
	Hydropres		Sulfachlorpyri-
	Reserpine		dazine
	Ser-Ap-Es		Sulfadimethoxine
			Sulfamerazine
			Sulfameter
			Sulfamethizole

<u>Message Code</u>	<u>Drug</u>
	Sulfamethoxazole
	Sulfamethoxypy- ridazine
	Sulfapyridine
	Sulfisoxazole
04782	Chlortetracycline
	Demethylchlortet- racycline
	Doxycycline
	Methacycline
	Oxytetracycline
	Tetracycline
04820	Aldactazide
	Bendroflumethiazide
	Benzthiazide
	Chlorothiazide
	Cyclothiazide
	Diupres
	Dyazide
	Hydrochlorothiazide
	Hydroflumethiazide
	Hydropres
	Methyclorthiazide
	Polythiazide
	Ser-Ap-Es
	Trichlormethiazide
04863	Liothyronine
	Liotrix
	Levothyroxine
	Thyroid
	Thyroglobulin

APPENDIX IV

Selected References

1. Garb, S.: "Clinical Guide to Undesirable Drug Interactions and Interferences," Springer Company, New York, 1971, p. 18.
2. Field, J.B., et al: "Potentiation of acetohexamide hypoglycemia by phenylbutazone," New Eng. J. Med., 277:889, 1967.
3. Antlitz, A.M., et al: "Potentiation of oral anticoagulant therapy by acetaminophen," Curr. Ther. Res., 10:501, 1968.
4. Antlitz, A.M. and Awalt, L.F.: "A double blind study of acetaminophen used in conjunction with oral anticoagulant therapy," Curr. Ther. Res., 11:360, 1969.
5. Gerhardt, R.E., et al: "Quinidine excretion in aciduria and alkaluria," Ann. Int. Med., 71:927, 1969.
6. Goodman, L.S. and Gilman, A.: "The Pharmacological Basis of Therapeutics," 4th Ed., Macmillan Co., New York, 1970, pp. 1253-1268.
7. Stuart, D.M.: "Drug metabolism Part II. Drug interactions," Pharmindex, 1968, pp. 1-14.
8. Goodman, L.S. and Gilman, A.: Op. cit., p. 889.
9. Godwin-Austin, R.B.: "Combined treatment of parkinsonism with l-dopa and amantadine," Lancet, 2:383, 1970.
10. Vesell, E.S.: "Impairment of drug metabolism in man by

- allopurinol and nortriptyline, " New Eng. J. Med., 283: 1484, 1970.
11. Mercaptopurine, Product Information, Burroughs Wellcome, 1971.
 12. Sawyer, N.J., et al.: "A Documented, Cross-Indexed Manual to Human Drug Interactions," 2nd Ed., University of Alabama, Birmingham, Alabama, 1971, p. 9.
 13. Hansten, P.D.: "Drug Interactions," Lea and Febriger, Philadelphia, 1971, p. 28.
 14. Garb, S.: Op. cit., p. 54.
 15. Klinenberg, M.F.: "Effect of corticosteroids on blood salicylate concentration," J. Am. Med. Assoc., 194: 601, 1965.
 16. Methotrexate, Product Information, Lederle Laboratories, 1970.
 17. Hansten, P.D.: Op. cit., p. 65.
 18. Yu, T.F., et al., "Mutual suppression of the uricosuric effects of sulfinpyrazone and salicylates: A study in interactions between drugs," J. Clin. Invest., 42: 1330, 1963.
 19. Robinson, W.D. "Current status of the treatment of gout," J. Am. Med. Assoc., 164: 1670, 1957.
 20. Krisko, I., et al., "Severe hyperpyrexia due to tranlycypromine-amphetamine toxicity," Ann. Int. Med., 70: 559, 1969.

21. Lockett, M.F. and Milner, G.: "Combining the antidepressant drugs," Brit. Med. J., 1: 921, 1965.
22. Cooper, A.J. and Ashcroft, G.: "Modification of insulin and sulfonylurea hypoglycemia by monoamine-oxidase inhibitor drugs," Diabetes, 16: 272, 1967.
23. Elis, J., et al.: "Modification by monoamine oxidase inhibitors of the effect of some sympathomimetics on blood pressure," Brit. Med. J., 2: 75, 1967.
24. Hansten, P.D.: "Op. cit.", p. 170-171.
25. Sjoqvist, F.: "Psychotropic drugs. Interaction between monoamine oxidase inhibitors and other substances," Proc. Roy. Soc. Med., 58: 967, 1965.
26. Parker, W.J.: "Clinically significant alcohol drug interactions," J. Amer. Pharm. Assoc., 10: 664, 1970.
27. Shafer, N.: "Hypotension due to nitroglycerin combined with alcohol," New Eng. J. Med., 273: 1169, 1965.
28. Udall, J.A.: "Drug interference with warfarin therapy (abst.)," Amer. J. Cardiol., 23: 143, 1969.
29. Goodman, L.S. and Gilman, A.: Op. cit., pp. 135-145.
30. Goodman, L.S. and Gilman, A.: Op. cit., pp. 146-148.
31. Penick, S.B., et al.: "Metronidazole in the treatment of alcoholism," Amer. J. Psychiat., 125: 1063, 1969.
32. Shelburne, P.F., et al.: "Guanethidine in combination with

- with hydralazine and with hydrochlorothiazide in hypertension," Amer. J. Med. Sci., 247: 307, 1964.
33. Sjoqvist, F. "The pH-dependent excretion of monomethylated tricyclic antidepressants in dogs and man," Clin. Pharmacol. Therap. 10: 826, 1969.
34. "The Medical Letter on Drugs and Therapeutics," Drug and Therapeutic Inc., New York, 11: 47, 1960.
35. Prange, A.J., et al.: "Enhancement of imipramine antidepressant activity by thyroid hormone," Amer. J. Psychiat., 126: 457, 1969.
36. Stone, C.A., et al.: "Antagonism of certain effects of catecholamine-depleting agents by antidepressant and related drugs," J. Pharmacol. Exp. Ther., 144: 196, 1964.
37. Milne, M.D.: "Influence of acid-base balance on efficacy and toxicity of drugs," Proc. Roy. Soc. Med., 58: 961, 1965.
38. Hansten, P.D.: Op. cit., p. 183.
39. Robinson, D.S. and Sylvester, D.: "Interaction of commonly prescribed drugs and warfarin," Ann. Int. Med., 72: 853, 1970.
40. Gualati, O.D., et al.: "Antagonism of adrenergic neuron blockade in hypertensive subjects," Clin. Pharmacol. Ther., 7: 510, 1966.
41. Espelin, D.E. and Done, A.K.: "Amphetamine poisoning:

- Effectiveness of chlorpromazine, " New Eng. J. Med., 278: 1361, 1968.
42. Rowland, M. "Amphetamine blood and urine levels in man, " J. Pharm. Sci., 58: 508, 1969.
43. Gilbaldi, M. and Schwartz, M.A.: "Apparent effect of probenecid on the distribution of penicillins in man, " Clin. Pharmacol. Therap., 9: 345, 1968.
44. Rado, J.P.: "Studies on the sites of action of ethacrynic acid and furosemide during angiotensin infusion, " J. Clin. Pharmacol. J. New Drugs, 10: 375, 1970.
45. Cucinell, S.A., et al.: "Drug interactions in man. Lowering effect of phenobarbital on plasma levels of bishydroxycoumarin and diphenylhydantoin, " Clin. Pharmacol. Ther., 6:420, 1965.
46. Kutt, H., et al.: "The effect of phenobarbital upon diphenylhydantoin metabolism in man (abst.), " Neurology, 15: 274, 1965.
47. Busfield, D. et al.: "An effect of phenobarbitone on blood-levels of griseofulvin in man, " Lancet, 2: 1042, 1963.
48. Procarbazine, Product Information, Roche Laboratoires, 1969.
49. MacDonald, M.G., et al.: "The effects of phenobarbital, chloral betaine, and glutethimide administration on warfarin plasma levels and hypoprothrombinemic responses in man, "

Clin. Pharmacol. Ther., 10: 80, 1969.

50. Hansen, J.M., et al.: "Dicumarol-induced diphenylhydantoin," Lancet, 2: 265, 1966.
51. Kristensen, M. and Hansen, J.M.: "Potentiation of the tolbutamide effect of Dicumarol," Diabetes, 16: 211, 1967.
52. Kristensen, M. and Hansen, J.M.: "Accumulation of chlorpropamide caused by Dicumarol," Acta. Med. Scand., 183, 1968.
53. Jeremy, R. and Towson, J.: "Interaction between aspirin and indomethacin in the treatment of rheumatoid arthritis," Med. J. Australia., 2: 127, 1970.
54. Zirkle, G.A., et al.: "Effects of chlorpromazine and alcohol on coordination and judgement," J. Am. Med. Assoc., 171: 1496, 1959.
55. Goodman, L.S. and Gilman, A.: Op. cit., pp. 98-120.
56. Gundersen, T., et al.: "Treatment of gonorrhoea by one oral dose of ampicillin and probenecid combined," Brit. J. Veneral. Dis., 45: 235, 1969.
57. Blackwell, B., et al.: "Hypertensive interactions between monoamine oxidase inhibitors and foodstuffs," Brit. J. Psychiat., 113: 349, 1967.
58. Goodman, L.S. and Gilman, A.: Op. cit., pp. 1371-1375.
59. Landauer, A.A., et al.: "Alcohol and amitriptyline effects

- on skills related to driving behavior," Science, 163: 1467, 1969.
60. Mitchell, J.R., et al.: "Antagonism of the antihypertensive action of guanethidine sulfate by desipramine hydrochloride," J. Am. Med. Assoc., 202: 973, 1967.
61. Leishman, A.W., et al.: "Antagonism of guanethidine by imipramine," Lancet, 1: 112, 1963.
62. Meyer, J.F., et al.: "Insidious and prolonged antagonism of guanethidine by amitriptyline," J. Am. Med. Assoc., 213: 1487, 1970.
63. Schrogie, J.J. and Solomon, H.M.: "The anticoagulant response to bishydroxycoumarin. II. The effect of d-thyroxine, clofibrate, and norethandrolone," Clin. Pharmacol. Ther., 8: 70, 1967.
64. Kippel, A.P. and Pitsinger, B.: "Hypothrombinemia secondary to antibiotic therapy and manifested by massive gastrointestinal hemorrhage," Arch. Surg., 96: 266, 1968.
65. Sellers, E.M. and Koch-Weser, J.: "Displacement from albumin and potentiation of warfarin by five acidic drugs," Clin. Res., 18, 344, 1970.
66. Sellers, E. and Koch-Weser, J.: "Potentiation of warfarin-induced hypoprothrombinemia by chloral hydrate," New Eng. J. Med., 283: 827, 1970.

67. Christensen, L.K. and Skovsted, L.: "Inhibition of drug metabolism by chloramphenicol," Lancet, 2: 1397, 1969.
68. Gross, L. and Brotman, M.: "Hypoprothrombinemia and hemorrhage associated with cholestyramine therapy," Ann. Int. Med., 72: 95, 1970.
69. Hansten, P.D.: Op. cit., p. 21.
70. Hunninghake, D.B. and Azarnoff, D.L.: "Drug interactions with warfarin," Arch. Int. Med., 121: 349, 1968.
71. Hansten, P.D.: Op. cit., p. 23.
72. Carter, S.A.: "Potentiation of the effect of orally administered anticoagulants by phenylamidol HCl," New Eng. J. Med., 273: 423, 1965.
73. Cullen, S.I. and Catalano, P.M.: "Griseofulvin-warfarin antagonism," J. Am. Med. Assoc., 199: 582, 1967.
74. Smith, J.W. (Ed.): "Manual of Medical Therapeutics," 19th Ed., Little, Brown and Co., Boston, 1969, p. 46.
75. Goodman, L.S. and Gilman, A.: Op. cit., pp. 677-708.
76. Applestein, J.M., et al.: "In vitro antimicrobial activity and human pharmacology of cephaloglycin," Appl. Microbiol., 16: 1006, 1968.
77. Alavi, I.A. and Pillay, V.K.: "Steroid-induced diabetic ketoacidosis (Abst.)," Ann. Int. Med., 72: 787, 1970.
78. Knouss, R.F., et al.: "Variation in quinidine excretion with

- changing urine pH (abst.), " Ann. Int. Med., 68: 1157, 1968.
79. Methenamine Mandelate, Product Information, Warner-Chilcott Laboratories, 1968.
80. Thomsen, K. and Schou, M.: "Renal lithium excretion in man," Amer. J. Physiol., 215: 823, 1968.
81. Hansten, P.D.: Op. cit., p. 96.
82. Miller, R.P. and Bates, J.H.: "Amphotericin B toxicity. A follow-up report of 53 patients," Ann. Int. Med., 71: 1089, 1969.
83. Goodman, L.S. and Gilman, A.: Op. cit., pp. 711-719.
84. Propranolol, Product Information, Ayerst Laboratories, 1969.
85. Cotzias, G.C., et al.: "L-dopa in Parkinson's syndrome," New Eng. J. Med., 281: 272, 1969.
86. Giles, T.D. and Modlin, R.K.: "Death associated with ventricular arrhythmia and thioridazine HCl," J. Am. Med. Assoc., 205: 108, 1968.
87. Spenney, J.G., et al.: "Hyperglycemic, hyperosmolar, nonketoacidotic diabetes: A complication of steroid and immunosuppressive therapy," Diabetes, 18: 107, 1969.
88. Gupta, K.K. and Lillicrap, C.A.: "Guanethidine and diabetes (Letter)," Brit. Med. J., 2: 697, 1968.
89. Gupta, K.K.: "Guanethidine and glucose tolerance in diabetes (Letter)," Brit. Med. J., 21: 679, 1968.

90. Kunin, C.M. and Finland, M.: "Clinical pharmacology of the tetracycline antibiotics," Clin. Pharmacol. Therap., 2: 51, 1961.
91. Hansten, P.D.: Op. cit., p. 134.
92. Searcy, R.L., et al.: "Blood clotting anomalies associated with intensive tetracycline therapy," Clin. Res., 12: 230, 1964.
93. Kuzucu, E.Y.: "Methoxyflurane, tetracycline, and renal failure," J. Am. Med. Assoc., 211: 1162, 1970.
94. Smith, J.W. (Ed.): Op. cit., pp. 96-105.
95. Seller, R.H., et al.: "Digitalis toxicity and hypomagnesemia," Amer. Heart. J., 79: 57, 1970.
96. Koch-Weser, J., et al.: "Adverse effects of sodium colistimethate. Manifestations and specific reaction rates during 317 courses of therapy," Ann. Int. Med., 72: 857, 1970.
97. Pittinger, C.B., et al.: "Antibiotic-induced paralysis," Anesth. Analg., 49: 487, 1970.
98. Schrogie, J.J., et al.: "Effect of oral contraceptives on vitamin K-dependent clotting activity," Clin. Pharmacol. Ther., 8: 670, 1967.
99. Spangler, A.S., et al.: "Enhancement of the antiinflammatory action of hydrocortisone by estrogen," J. Clin. Endocr., 29: 650, 1969.
100. Werk, E.E., et al.: "Interference in the effect of dexamethasone

- by diphenylhydantoin, " New Eng. J. Med., 281: 32, 1969.
101. Jubiz, W., et al.: "Effect of diphenylhydantoin on the metabolism of dexamethasone. Mechanism of the abnormal dexamethasone suppression in humans, " New Eng. J. Med., 283: 11, 1970.
102. Thorn, G.W.: "Clinical considerations in the use of corticosteroids, " New Eng. J. Med., 274: 775, 1966.
103. Goodwin, C.S. and Sparell, G.: "Inhibition of dapsone excretion by probenecid, " Lancet, 2: 884, 1969.
104. Kater, R.M., et al.: "Increased rate of clearance of drugs from the circulation of alcoholics, " Amer. J. Med. Sci., 258: 35, 1969.
105. Olesen, O.V.: "The influence of disulfiram and calcium carbimide on the serum diphenylhydantoin, " Arch. Neurol., 16: 642, 1967.
106. Kutt, H., et al.: "Diphenylhydantoin intoxication. A complication of isoniazid therapy, " Amer. Rev. Resp. Dis., 101: 337, 1970.
107. Murray, F.J.: "Outbreak of unexpected reactions among epileptics taking isoniazid, " Amer. Rev. Resp. Dis., 86: 729, 1962.
108. Hartshorn, E.A.: "Drug interactions: Antineoplastics, " Drug Intell. and Clin. Pharm., 3: 196, 1969.

109. Solomon, H. M. and Schrogie, J. J.: "The effect of phenyramidol on the metabolism of diphenylhydantoin," Clin. Pharmacol. Ther., 8:554, 1967.
110. Berger, S.: "Platelet function: A review. Part II. Abnormal function," Canad. Med. Assoc. J., 102:1379, 1970.
111. Whittington, H. G. and Grey, L.: "Possible interaction between disulfiram and isoniazid," Amer. J. Psychiat., 125:1725, 1969.
112. Rothstein, E. and Clancy, D. D.: "Toxicity of disulfiram combined with metronidazole," New Eng. J. Med., 280:1006, 1969.
113. Goodhue, W. W.: "Disulfiram-metronidazole toxicity," New Eng. J. Med., 280:1482, 1969.
114. Cavallaro, R. J., et al.: "Effect of ecothiophate therapy on metabolism of succinylcholine in man," Anesth. Analg., 47: 570, 1968.
115. Smith, J. W. (Ed.): Op. cit., p. 317.
116. Mathog, R. H. and Klein, W. J.: "Ototoxicity of ethacrynic acid and aminoglycoside antibiotics in uremia," New Eng. J. Med., 280:1223, 1969.
117. Johansson, S.: "Apparent resistance to oral anticoagulant therapy and influence of hypnotics on some coagulation factors," Acta. Med. Scand., 184: 297, 1968.

118. Eastham, R.D. and Griffiths, E.P.: "Reduction of platelet adhesiveness and prolongation of coagulation time of activated plasma by glyceryl guaiacolate," Lancet, 1: 795, 1965.
119. Furosemide, Product Information, Hoechst Pharmaceutical Co., 1969.
120. Garamycin, Product Information, Schering Corporation, 1969.
121. Methotrimeprazine, Product Information, Lederle Laboratories, 1966.
122. Desmankar, B.S. and Lewis, J.A.: "Ventricular tachycardia associated with the administration of methylphenidate during guanethidine therapy," Canad. Med. Assoc. J., 97: 1166, 1967.
123. Methylphenidate, Product Information, CIBA Pharmaceutical Co., 1970.
124. Sneddon, J.M. and Turner, P. "The interactions of local guanethidine and sympathomimetic amines in the human eye," Arch. Ophthal., 81: 622, 1969.
125. Goodman, L.S. and Gilman, A.: Op. cit., pp. 719-722.
126. Waal, H.J.: "Hypotensive action of propranolol," Clin. Pharmacol. Ther., 7: 588, 1966.
127. Goodman, L.S. and Gilman, A.: Op. cit., 711-719.
128. Skeith, M.D., et al.: "The renal excretion of indomethacin and its inhibition by probenecid," Clin. Pharmacol. Ther.,

99: 89, 1968.

129. Arky, R.A.: "Irreversible hypoglycemia. A complication of alcohol and insulin," J. Am. Med. Assoc., 206:575, 1968.
130. Meyler, L. (Ed.): "Side Effects of Drugs," 4th Ed., Excerpta Medica Foundation, Amsterdam, 1964, pp. 137-141.
131. Meperidine HCl, Product Information, Winthrop Laboratories, 1969.
132. Michaelis, E. and Rosen, A.: "Depression of isoprenaline-induced idioventricular rhythm in man by betaadrenergic receptor blocking agents," Acta. Med. Scand., 183:401, 1968.
133. McCall, C.E., et al.: "Lincomycin: activity in vitro and absorption and excretion in normal young men," Amer. J. Med. Sci., 254:144, 1967.
134. Thomsen, K. and Schou, M.: "Renal lithium excretion in man," Amer. J. Physiol., 215:823, 1968.
135. Platman, S.R. and Fieve, R.R.: "Lithium retention and excretion. The effect of sodium and fluid intake," Arch. Gen. Psychiat., 20:285, 1969.
136. Friend, D.G., et al.: "The action of l-dihydroxyphenylalanine in patients receiving nialamide," Clin. Pharmacol. Ther., 6:362, 1965.
137. Cotzias, G.C., et al.: "L-dopa in Parkinson's syndrome (Letter)," New Eng. J. Med., 281:272, 1969.

138. Duvoisin, R.C., et al.: "Pyridoxine reversal of l-dopa effects in parkinsonism," Trans. Amer. Neurol. Assoc., 94: 81, 1969.
139. Cotzias, G.C.: "Metabolism modification of some neurologic disorders," J. Am. Med. Assoc., 210: 1255, 1969.
140. Allopurinol, Product Information, Burroughs Wellcome and Co., 1970.
141. Hall, G.J. and Davis, A.E.: "Inhibition of iron absorption by magnesium trisilicate," Med. J. Aust., 2: 95, 1969.
142. Ghoneim, M.M. and Long, J.P.: "The interaction between magnesium and other neuromuscular blocking agents," Anesthesiology, 32: 23, 1970.
143. Methenamine Mandelate, Product Information, Warner-Chilcott Laboratories, 1968.
144. Meyers, F.H., et al.: "Review of Medical Pharmacology," 2nd. Ed., Lange Medical Publications, Los Altos, California, 1970, pp. 494-497.
145. Lipton, J.H.: "Sulfamethizole and methenamine incompatibility," New Eng. J. Med., 2: 92, 1963.
146. Dixon, R.L., et al.: "Plasma protein binding of methotreate and its displacement by various drugs," Fed. Proc., 24: 452, 1965.
147. Liegler, D.G., et al.: "The effect of organic acids on renal

- clearance of methotrexate in man," Clin. Pharmacol. Ther., 10: 849, 1969.
148. Allison, J.: "Methotrexate and smallpox vaccination (Letter)," Lancet, 2: 1250, 1968.
149. Methotrimeprazine, Product Information, Lederle Laboratories, 1966.
150. Waal, H.J. "Hypotensive action of propranolol," Clin. Pharmacol. Ther., 7: 588, 1966.
151. Methylphenidate, Product Information, CIBA Pharmaceuticals, 1970.
152. Meyers, F.H., et al.: Op. cit., pp. 105-109.
153. Schelling, J.L. and Lasagna, L.: "A study of cross-tolerance to circulating effects of organic nitrates," Clin. Pharmacol. Ther., 8: 256, 1967.
154. Gibaldi, M. and Schwartz, M.A.: "Apparent effect of probenecid on the distribution of penicillins in man," Clin. Pharmacol. Ther., 9: 345, 1968.
155. Hvidberg, E.F., et al.: "Studies of the interaction of phenylbutazone, oxyphenbutazone and methandrostenolone in man," Proc. Soc. Exp. Biol. Med., 129: 438, 1968.
156. Weiner, M., et al.: "Effect of steroids on disposition of oxyphenbutazone in man," Proc. Soc. Exp. Biol. Med., 124: 1170, 1967.

157. Goodman, L.S. and Gilman, A.: Op. cit., pp. 98-120.
158. Fletcher, G.F., et al.: "Cardiotoxic effects of Mellaril: Conduction disturbances and supraventricular arrhythmias," Amer. Heart J., 78:135, 1969.
159. Goodman, L.S. and Gilman, A.: Op. cit., pp. 155-169.
160. Giles, T.D. and Modlin, R.K.: "Death associated with ventricular arrhythmia and thioridazine hydrochloride," J. Am. Med. Assoc., 205:108, 1968.
161. Sadove, M.S., et al.: "The potentiating action of chlorpromazine," Anesth. Analg., 35:165-181, 1956.
162. Solomon, H.M. and Schrogie, J.J.: "Effect of phenyramidol and bishydroxycoumarin on the metabolism of tolbutamide in human subjects," Metabolism, 16:1029, 1967.
163. Malinis, J.M.: "Diuretics in diabetes mellitus (Letter)," Practitioner, 201:529, 1968.
164. Tranquada, R.E.: "Diuretics for diabetic patient taking an oral hypoglycemic agent (Letter)," J. Am. Med. Assoc., 206:1580, 1968.
165. Slade, I.H. and Iosefa, R.N.: "Fatal hypoglycemic coma from the use of tolbutamide in elderly patients: report of two cases," J. Am. Geriatr. Soc., 15: 948, 1967.
166. Kotler, M.N., et al.: "Hypoglycemia precipitated by propranolol," Lancet, 2:1389, 1966.

167. Abramson, E.A. and Arky, R.A.: "Role of beta-adrenergic receptors in counterregulation to insulin-induced hypoglycemia," Diabetes, 17: 141, 1968.
168. Smith, J.W.: Op. cit., pp. 119-122.
169. Orphenadrine, Product Information, Riker Laboratories, 1969.
170. Propoxyphene, Product Information, Eli Lilly and Co., 1969.
171. Dreifus, L.S., et al.: "Propranolol and quinidine in the management of ventricular tachycardia," J. Am. Med. Assoc., 204: 736, 1968.
172. Stern, S.: "Synergistic action of propranolol with quinidine," Amer. Heart J., 72: 569, 1966.
173. Schmidt, J.L., et al.: "The effect of quinidine on the action of muscle relaxants," J. Am. Med. Assoc., 183: 669, 1963.
174. Hydrochlorothiazide, Product Information, CIBA Pharmaceutical Co., 1969.
175. Milne, M.D.: "Influence of acid-base balance on the efficacy and toxicity of drugs," Proc. Roy. Soc. Med., 58: 961, 1965.
176. Schroeder, E.T.: "Alkalosis resulting from combined administration of a non-systemic antacid and a cation-exchange resin," Gastroenterology, 56: 868, 1969.
177. Northcutt, R.C., et al.: "The influence of cholestyramine on thyroxin absorption," J. Am. Med. Assoc., 208: 1857, 1969.
178. Azarnoff, D.L. and Hurwitz, A.: "Drug interactions,"

Pharmacol. Physicians, 4: 1, 1970.

179. Albert, M. and Stansell, M.J.: "Vascular symptomatic relief during administration of clofibrate," Metabolism, 18: 635, 1969.
180. Goldberg, L.: "Behavioral and physiological effects of alcohol on man," Psychosom. Med., 28: 570-595, 1966.
181. Zirkle, G.A.: "Meprobamate and small amounts of alcohol. Effects on human ability, coordination, and judgement," J. Am. Med. Assoc., 173: 1823-1825, 1960.
182. Bisacodyl, Product Information, Geigy Pharmaceuticals, 1971.
183. Neuvonen, P.J., et al.: "Interference of iron with the absorption of tetracycline in man," Brit. Med. J., 4: 509, 1970.
184. Osal, A., et al.: "The United States Dispensatory and Physicians' Pharmacology," 26th Ed., Lippincott, Philadelphia, 1967, p. 29.
185. Koch-Weser, J. "Quinidine-induced hypoprothrombinemic hemorrhage in patients on chronic warfarin therapy," Ann. Int. Med., 68: 511, 1968.
186. "The Medical Letter on Drugs and Therapeutics", Drug and Therapeutic Information Inc., New York, 12: 41, 1970.
187. Carbenicillin, Product Information, J.B. Roerig Division, 1971.
188. Landon, J., et al.: "The effect of anabolic steroids on blood sugar and plasma levels in man," Metabolism, 12: 924, 1963.

APPENDIX V

Drug-Drug Interaction Printout

ACETAMINOPHEN ELEVATES THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS.

ACETAZOLAMIDE (DIAMOX), URINARY ALKALINIZING AGENT, ELEVATES SERUM LEVELS OF AMPHETAMINES, TRICYCLIC ANTIDEPRESSANTS AND QUINIDINE BY ENHANCING RENAL REABSORPTION. IT MAY ANTAGONIZE THE ACTIVITY OF METHENAMINE COMPOUNDS.

ETHYL ALCOHOL-ADDITIVE EFFECTS MAY BE SEEN WITH CNS DEPRESSANTS AND ANTIHISTAMINES. IT MAY ANTAGONIZE THE PHARMACOLOGICAL EFFECTS OF THE ORAL ANTICOAGULANTS AND DIPHENYLHYDANTICIN. IT MAY ENHANCE THE ADVERSE EFFECTS OF GUANETHIDINE, NITROGLYCERIN, DISULFIRAM (ANTABUSE), METRONIDAZOLE (FLAGYL) AND TRICYCLIC ANTIDEPRESSANTS. IT PROLONGS THE ACTION OF INSULIN.

ALLOPURINOL POTENTIATES THE EFFECTS OF BISHYDROXYCOUMARIN, AND MERCAPTOPURINE. IT MAY INCREASE HEPATIC IRON CONCENTRATION.

ANTACIDS CONTAINING DIVALENT AND TRIVALENT CATIONS DECREASE ORAL ABSORPTION OF TETRACYCLINES. ANTACIDS SHOULD NOT BE ADMINISTERED SIMULTANEOUSLY WITH ENTERIC COATED PRODUCTS. SODIUM POLYSTYRENE RESIN (KAYEXALATE) BINDS MAGNESIUM AND CALCIUM IONS FOUND IN ANTACIDS RESULTING IN SYSTEMIC ALKALOSIS.

AMANTADINE (SYMMETREL) POTENTIATES THE PHARMACOLOGICAL EFFECTS PRODUCED BY LEVODOPA.

AMINOPHYLLIN MAY IMPAIR THE THERAPEUTIC RESPONSE TO LITHIUM CARBONATE BY INCREASING THE RENAL EXCRETION OF LITHIUM IONS.

AMINOSALICYLIC ACID PLASMA LEVELS ARE ELEVATED BY PROBENECID (BENEMID)

AMMONIUM CHLORIDE (URINARY ACIDIFIER) MAY DECREASE RENAL REABSORPTION OF AMPHETAMINES AND TRICYCLIC ANTIDEPRESSANTS.

AMPHOTERICIN B (FUNGIZONE) MAY PRODUCE HYPOKALEMIA PRECIPITATING DIGITALIS TOXICITY. IT MAY POTENTIATE NEUROMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS.

AMPICILLIN PLASMA LEVELS ARE INCREASED BY CONCOMITANT USE OF PROBENECID (BENEMID).

AMPHETAMINES POTENTIATE MAOI AND ANTAGONIZE THE EFFECTS OF GUANETHIDINE. PHENOTHIAZINES MAY ANTAGONIZE THE CENTRAL EFFECTS OF AMPHETAMINES. URINE ACIDIFYING AGENTS DECREASE RENAL REABSORPTION AND URINARY ALKALINIZERS SUCH AS ACETAZOLAMIDE (DIAMOX), SODIUM BICARBONATE AND THIAZIDE DIURETICS INCREASE REABSORPTION.

ANGIOTENSIN AMIDE (HYPERTENSIN)-INDUCED ANTIDIURESIS AND ANTINATRIURESIS IS REVERSED BY ETHACRYNIC ACID (EDECRIN) AND FUROSEMIDE (LASIX).

ANABOLIC STEROIDS MAY POTENTIATE THE ACTIVITY OF ORAL ANTICOAGULANTS, PHENYLBUTAZONE (BUTAZOLIDIN) AND OXYPHENBUTAZONE (TANDEARIL). THEY MAY DECREASE INSULIN REQUIREMENTS IN DIABETICS.

ANTICHOLINERGIC DRUGS MAY POTENTIATE QUINIDINE AND THE SECONDARY PHARMACOLOGICAL EFFECTS OF ANTIHISTAMINES AND TRICYCLIC ANTIDEPRESSANTS. PROPRANOLOL (INDERAL)-INDUCED ADVERSE EFFECTS ARE ANTAGONIZED BY ANTICHOLINERGICS. THEY MAY PRODUCE EXTRAPYRAMIDAL SYMPTOMS WHEN USED SIMULTANEOUSLY WITH METHOTRIMEPRAZINE (LEVOPROME).

ORAL ANTICOAGULANTS ARE POTENTIATED BY ACETAMINOPHEN, ESTROGENS, ANABOLIC STEROIDS, CHLORAMPHENICOL, CHOLESTYRAMINE (CUEPID), CLOFIBRATE (ATROMID S), D-THYROXINE, PHENYLBUTAZONE (BUTAZOLIDIN) AND PHENYRAMIDOL (ANALEXIN). THEY MAY BE POTENTIATED BY AMINOGLYCOSIDE ANTIBIOTICS, DI-PHENYLHYDANTICIN, INDOMETHACIN, QUINIDINE AND SALICYLATES. THEY ARE ANTAGONIZED BY ETHYL ALCOHOL, BARBITURATES, ETHCHLORVYNOL, GRISEOFULVIN AND GLUTETHIMIDE. THEY ARE VARIABLY AFFECTED BY CHLORAL HYDRATE.

TRICYCLIC ANTIDEPRESSANTS MAY POTENTIATE THE ADVERSE EFFECTS OF MAOI AND ETHYL ALCOHOL AND THE PHARMACOLOGICAL EFFECTS OF SYMPATHOMIMETICS, THYROID PREPARATIONS, ANTIHISTAMINES AND ANTICHOLINERGICS. THEY MAY ANTAGONIZE GUANETHIDINE. BARBITURATES APPEAR TO DECREASE THERAPEUTIC ACTIVITY. THEY ARE POTENTIATED BY METHYLPHENIDATE. URINE ACIDIFYING AGENTS DECREASE RENAL REABSORPTION AND URINE ALKALINIZING AGENTS INCREASE REABSORPTION.

ANTIHISTAMINES MAY PRODUCE ADDITIVE CNS DEPRESSANT EFFECTS WHEN USED CONCOMITANTLY WITH ETHYL ALCOHOL, BARBITURATES AND PHENOTHIAZINES. THEY MAY POTENTIATE THE PHARMACOLOGICAL ACTIVITY OF ANTICHOLINERGICS AND THE ADVERSE EFFECTS OF TRICYCLIC ANTIDEPRESSANTS.

ANTIHYPERTENSIVE AGENTS MAY BE POTENTIATED BY METHOTRIMEPAZINE (LEVOPROME), PROCAINAMIDE (PRONESTYL) AND PROPRANOLOL (INDERAL).

ASCORBIC ACID (URINARY ACIDIFIER) MAY ANTAGONIZE AMPHETAMINES AND TRICYCLIC ANTIDEPRESSANTS.

BARBITURATES-ADDITIVE EFFECTS MAY BE SEEN WITH THE CONCOMITANT USE OF ANTIHISTAMINES, PHENOTHIAZINES AND OTHER CNS DEPRESSANTS. THEY MAY BE POTENTIATED BY PROCARBAZINE (MATULANE). THEY MAY DECREASE THERAPEUTIC EFFECTS OF ORAL ANTICOAGULANTS, TRICYCLIC ANTIDEPRESSANTS AND GRISEOFULVIN. THEY MAY VARIABLY EFFECT SERUM DIPHENYLHYDANTOIN LEVELS.

BISHYDROXYCOUMARIN MAY POTENTIATE THE SULFONYLUREAS AND INCREASE SERUM LEVELS OF DIPHENYLHYDANTOIN. IT IS POTENTIATED BY ACETAMINOPHEN, ESTROGENS, ANABOLIC STEROIDS, CHLORAMPHENICOL, CHOLESTYRAMINE (CUEMID), CLOFIBRATE (ATROMID S), D-THYROXINE, PHENYLBUTAZONE (BUTAZOLIDIN) AND PHENYRAMIDOL (ANALEXIN). IT MAY BE POTENTIATED BY AMINOGLYCOSIDE ANTIBIOTICS, DIPHENYLHYDANTOIN, INDOMETHACIN AND SALICYLATES. IT IS ANTAGONIZED BY ETHYL ALCOHOL, BARBITURATES, ETHCHLORVYNOL, GRISEOFULVIN AND GLUTETHIMIDE. IT IS VARIABLY AFFECTED BY CHLORAL HYDRATE.

BISACODYL (DULCOLAX) TABLETS SHOULD NOT BE TAKEN CONCOMITANTLY WITH ANTACIDS.

CALCIUM ICNS ADMINISTERED PARENTERALLY MAY PHARMACOLOGICALLY POTENTIATE DIGITALIS GLYCOSIDES.

CARBENICILLIN (PYOPEN, GEOPEN) PLASMA LEVELS MAY BE ELEVATED AND PROLONGED BY PROBENECID (BENEMID).

CEPHALOSPORINS, ALL-PLASMA LEVELS ARE ELEVATED BY PROBENECID (BENEMID). CONCOMITANT ADMINISTRATION OF CEPHALOTHIN AND COLISTIN INCREASES INCIDENCE OF NEPHROTOXICITY.

CHLORAL BETAINE (BETA-CHLOR) VARIABLY EFFECTS THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS.

CHLORAL HYDRATE VARIABLY EFFECTS THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS.

CHLORAMPHENICOL MAY POTENTIATE ORAL ANTICOAGULANTS, DIPHENYLHYDANTOIN AND SULFONYLUREAS.

DIURETICS PRODUCING POTASSIUM AND MAGNESIUM DEFICIENCIES MAY PRECIPITATE DIGITALIS TOXICITY. CONCOMITANT USE WITH CORTICOSTEROIDS MAY RESULT IN EXCESSIVE POTASSIUM LOSS. DIURETICS MAY ANTAGONIZE THE ACTIVITY OF ORAL HYPOGLYCEMICS.

CHOLESTYRAMINE (QUEMID) MAY ELEVATE THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS. IT DECREASES ABSORPTION OF THYROID PREPARATIONS BY BINDING THYRAXINE AND TRIIODOTHYRONINE.

CLOFIBRATE (ATROMID S) PHARMACOLOGICALLY ELEVATES THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS. IT MAY INHIBIT PLATELET ADHESIVENESS.

COLISTIN (COLIMYCIN) ENHANCES NEUROMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS. CONCOMITANT ADMINISTRATION OF PARENTERAL CEPHALOSPORINS INCREASES INCIDENCE OF NEPHROTOXICITY.

CORTICOSTEROIDS MAY BE POTENTIATED BY ESTROGENS. THEY MAY PHARMACOLOGICALLY ANTAGONIZE HYPOGLYCEMICS AND DECREASE SALICYLATE PLASMA LEVELS. DIPHENYLHYDANTOIN MAY DECREASE THERAPEUTIC RESPONSE TO CORTICOSTEROIDS. CONCOMITANT USE WITH DIURETICS MAY RESULT IN EXCESSIVE POTASSIUM LOSS.

CORTICOTRCPIN (ACTH) MAY BE POTENTIATED BY ESTROGENS. IT MAY PHARMACOLOGICALLY ANTAGONIZE HYPOGLYCEMICS AND DECREASE SALICYLATE PLASMA LEVELS. DIPHENYLHYDANTOIN MAY DECREASE RESPONSE TO CORTICOSTEROIDS. CONCOMITANT USE WITH DIURETICS MAY RESULT IN EXCESSIVE POTASSIUM LOSS.

DAPSONE (AVLOSULFON) PLASMA LEVELS ARE INCREASED BY PROBENECID (BENEMID).

DIGITALIS GLYCOSIDES ARE PHARMACOLOGICALLY POTENTIATED BY PARENTERAL CALCIUM PREPARATIONS AND DIURETICS PRODUCING POTASSIUM AND MAGNESIUM DEFICIENCIES. AMPHOTERICIN B (FUNGIZONE) MAY PRODUCE HYPOKALEMIA PRECIPITATING DIGITALIS TOXICITY. SYMPATHOMIMETICS MAY INCREASE INCIDENCE OF CARDIAC ARRHYTHMIAS.

DIPHENYLHYDANTOIN IS POTENTIATED BY CHLORAMPHENICOL, DISULFIRAM (ANTABUSE) AND ISONIAZID. IT MAY BE ANTAGONIZED BY ETHYL ALCOHOL AND PHENYRAMIDOL (ANALEXIN). IT MAY POTENTIATE ORAL ANTICOAGULANTS AND METHOTREXATE. IT MAY DECREASE THE THERAPEUTIC RESPONSE TO CORTICOSTEROIDS.

CIPYRIDAMCLE (PERSANTINE) MAY POTENTIATE THE ANTICOAGULANT ACTIVITY OF HEPARIN.

DISULFIRAM (ANTABUSE) POTENTIATES DIPHENYLHYDANTOIN. CONCOMITANT USE WITH ISONIAZID, ETHYL ALCOHOL AND METRONIDAZOLE (FLAGYL) ENHANCES THE INCIDENCE OF ADVERSE EFFECTS.

ECFOTHIOPHATE IODIDE (PHOSPHOLINE IODIDE) POTENTIATES THE PHARMACOLOGICAL EFFECTS OF SUCCINYLCHOLINE.

EPHEDRINE POTENTIATES HYPERTENSIVE REACTIONS WITH MAOI. IT ANTAGONIZES THE ADRENERGIC NEURON BLOCKADE PRODUCED BY GUANETHIDINE (ISMELIN).

EPINEPHRINE, AND TO A LESSER EXTENT, OTHER ADRENERGIC AGENTS MAY DECREASE ACTIVITY OF HYPOGLYCEMIC AGENTS.

ESTROGENS PHARMACOLOGICALLY ELEVATE THE ANTICOAGULANT ACTIVITY OF ORAL ANTICOAGULANTS. THEY MAY POTENTIATE CORTICOSTEROID ACTIVITY.

ETHACRYNIC ACID POTENTIATES OTOTOXICITY OF AMINOGLYCOSIDE ANTIBIOTICS. IT MAY PRODUCE POTASSIUM AND MAGNESIUM DEFICIENCIES PRECIPITATING DIGITALIS TOXICITY. CONCOMITANT USE WITH CORTICOSTEROIDS MAY ENHANCE POTASSIUM LOSS. IT MAY ANTAGONIZE THE ACTIVITY OF ORAL HYPOGLYCEMICS.

ETHCHLORVYNOL (PLACIDYL) ANTAGONIZES THE ANTICOAGULANT ACTIVITY OF ORAL ANTICOAGULANTS.

FOLIC ACID ANTAGONIZES THE ANTINEOPLASTIC ACTIVITY OF METHOTREXATE.

FUROSEMIDE MAY PRODUCE POTASSIUM AND MAGNESIUM DEFICIENCIES PRECIPITATING DIGITALIS TOXICITY. CONCOMITANT USE WITH CORTICOSTEROIDS MAY ENHANCE POTASSIUM LOSS. IT ENHANCES THE EFFECTS OF TUBOCURARINE. IT MAY ANTAGONIZE THE ACTIVITY OF ORAL HYPOGLYCEMICS.

GENTAMICIN IN COMBINATION WITH OTHER AMINOGLYCOSIDE ANTIBIOTICS INCREASES INCIDENCE OF OTOTOXICITY AND NEPHROTOXICITY. ETHACRYNIC ACID POTENTIATES THE OTOTOXICITY. IT ENHANCES THE BLOCKADE OF SKELETAL MUSCLE RELAXANTS.

GLUTETHIMIDE (DORIDEN) DECREASES ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS.

GLYCERYL GUAIACOLATE MAY POTENTIATE THE ANTICOAGULANT ACTIVITY OF HEPARIN.

GRISEOFULVIN MAY DECREASE THE ANTICOAGULANT ACTIVITY OF ORAL ANTI-COAGULANTS. IT IS ANTAGONIZED BY BARBITURATES WHICH MAY IMPAIR ABSORPTION.

GUANETHIDINE MAY BE POTENTIATED BY PROCAINAMIDE, PROPRANOLOL AND QUINIDINE. IT IS ANTAGONIZED BY AMPHETAMINES, TRICYCLIC ANTIDEPRESSANTS, EPHEDRINE AND METHYLPRENIDATE. IT MAY POTENTIATE PHENYLEPHRINE AND DECREASE ACTIVITY OF HYPOGLYCEMICS. ETHYL ALCOHOL AND METHOTRIMEPAZINE (LEVOPROME), PROCARBAZINE (MATULANE) AND THIAZIDE DIURETICS MAY POTENTIATE ORTHOSTATIC HYPOTENSION.

HEPARIN INDUCED ANTICOAGULANT ACTIVITY MAY BE ENHANCED BY DIPYRIDAMOLE (PERSANTINE) AND GLYCERYL GUAIACOLATE.

ORAL HYPOGLYCEMIC AGENTS MAY BE POTENTIATED BY CHLORAMPHENICOL, MAOI, PHENYLBUTAZONE (BUTAZOLIDIN), PROPRANOLOL (INDERAL), BISHYDROXYCOUMARIN, PHENYRAMIDOL (ANALEXIN) AND SALICYLATES. THE HYPOGLYCEMIC EFFECTS ARE ANTAGONIZED BY CORTICOSTEROIDS, DIURETICS AND GUANETHIDINE (ISMELIN).

INDOMETHACIN MAY PHARMACOLOGICALLY ELEVATE THE ACTIVITY OF ORAL ANTI-COAGULANTS. INDOMETHACIN PLASMA LEVELS MAY BE INCREASED BY PROBENECID (BENEMID) AND DECREASED BY SALICYLATES.

INSULIN MAY BE PHARMACOLOGICALLY ANTAGONIZED BY GUANETHIDINE. ETHYL ALCOHOL MAY PROLONG THE ACTION OF INSULIN. GLUCOCORTICOID, THYROID, EPINEPHRINE AND THIAZIDE DIURETICS MAY INCREASE INSULIN REQUIREMENTS.

IRON SALTS SHOULD NOT BE USED SIMULTANEOUSLY WITH ALLOPURINOL (ZYLUPRIM). ANTACIDS MAY DECREASE IRON ABSORPTION. IRON SALTS MAY IMPAIR THE ABSORPTION OF ORAL TETRACYCLINES.

ISONIAZID INCREASES PLASMA LEVELS OF DIPHENYLHYDANTOIN. IT MAY BE ANTAGONIZED BY ETHYL ALCOHOL. CONCOMITANT USE WITH DISULFIRAM (ANTABUSE) AND MEPERIDINE ENHANCES INCIDENCE OF ADVERSE EFFECTS.

D-THYROXINE ELEVATES THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS.

ISOPROTERENOL IS PHARMACOLOGICALLY ANTAGONIZED BY PROPRANOLOL (INDERAL)

KANAMYCIN IN COMBINATION WITH OTHER AMINOGLYCOSIDE ANTIBIOTICS INCREASES INCIDENCE OF OTOTOXICITY AND NEPHROTOXICITY. CONCOMITANT USE WITH ETHACRYNIC ACID POTENTIATES THE OTOTOXICITY. IT POTENTIATES NEUROMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS. WHEN ADMINISTERED BY THE ORAL ROUTE IT MAY INCREASE THE ACTIVITY OF ORAL ANTICOAGULANTS.

KAOLIN-PECTIN MIXTURES INHIBIT THE ABSORPTION OF ORALLY ADMINISTERED LINCOMYCIN (LINCOCIN).

LEVODOPA MAY BE ANTAGONIZED BY METHYLDOPA, PYRIDOXINE, RESERPINE AND PHENOTHIAZINES. CONCOMITANT USE WITH MAOI MAY PRODUCE HYPERTENSION. ADDITIVE THERAPEUTIC EFFECTS MAY OCCUR WITH AMANTADINE (SYMMETREL).

LITHIUM EXCRETION IS INCREASED BY AMINOPHYLLINE, SODIUM BICARBONATE AND LARGE DOSES OF SODIUM CHLORIDE. LOW SODIUM INTAKE MAY PRECIPITATE LITHIUM TOXICITY.

MAGNESIUM IONS ADMINISTERED PARENTERALLY POTENTIATE THE NEURCMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS.

MEPERIDINE SHOULD NOT BE USED SIMULTANEOUSLY WITH ISONIAZID AND MAOI- IT ENHANCES INCIDENCE OF ADVERSE EFFECTS. IT IS POTENTIATED BY OTHER CNS DEPRESSANTS.

MEPROBAMATE (EQUANIL, MILTOWN) IS POTENTIATED BY ETHYL ALCOHOL.

MERCAPTOPURINE (PURINETHOL) IS POTENTIATED BY ALLOPURINOL (ZYLOPRIM).

METARAMINCL (ARAMINE) IS PHARMACOLOGICALLY POTENTIATED BY MAOI.

METHENAMINE COMPOUNDS EXHIBIT OPTIMUM ACTIVITY IN A URINE PH OF 5.5 OR LOWER. URINE ACIDIFYING AGENTS ARE USEFUL ADJUNCTS WHILE URINE ALKALINIZERS DECREASE ACTIVITY. CONCOMITANT USE WITH SULFONAMIDES FREQUENTLY, RESULTS IN CRYSTALLURIA AND THE FORMATION OF A PRECIPITATE.

METHOTREXATE SERUM LEVELS ARE ELEVATED BY DIPHENYLHYDANTOIN, SALICYLATES AND SULFONAMIDES. IT MAY IMPAIR THE IMMUNOLOGICAL RESPONSE TO SMALLPOX VACCINE, RESULTING IN VACCINA.

METHOTRIMEPAZINE (LEVOPROME) POTENTIATES THE EFFECTS OF ANTIHYPER- TENSIVE AGENTS, OTHER CNS DEPRESSANTS AND SKELETAL MUSCLE RELAXANTS. IT WILL PRODUCE EXTRAPYRAMIDAL SYMPTOMS WHEN USED SIMULTANEOUSLY WITH ANTICHOLINERGICS.

METHYOXYFLURANE ANESTHESIA IN CONJUNCTION WITH TETRACYCLINE THERAPY INCREASES INCIDENCE OF NEPHROTOXIC EFFECTS.

METHYLDOPA MAY ANTAGONIZE THE THERAPEUTIC EFFECTS OF LEVODOPA. ADDITIVE HYPOTENSIVE EFFECTS MAY OCCUR WITH PROPRANOLOL (INDERAL), PROCAINAMIDE (PRONESTYL), METHOTRIMEPAZINE (LEVOPROME) AND THIAZIDE DIURETICS.

METHYLPHENIDATE (RITALIN) POTENTIATES TRICYCLIC ANTIDEPRESSANTS. IT MAY BE POTENTIATED BY MAOI. IT ANTAGONIZES THE PHARMACOLOGICAL EFFECTS OF GUANETHIDINE (ISMELIN).

METRONIDAZOLE (FLAGYL) SHOULD NOT BE USED SIMULTANEOUSLY WITH DISULFIRAM (ANTABUSE) OR ETHYL ALCOHOL DUE TO THE INCREASED INCIDENCE OF ADVERSE EFFECTS.

MONOAMINE OXIDASE INHIBITORS POTENTIATE THE PHARMACOLOGICAL EFFECTS OF AMPHETAMINES, METHYLPHENIDATE (RITALIN), TRICYCLIC ANTIDEPRESSANTS, HYPOLYCEMICS AND SYMPATHOMIMETICS SUCH AS EPHEDRINE, METARAMINOL (ARAMINE), PHENYLEPHRINE AND PHENYLPROPANOLAMINE. CONCOMITANT USE WITH MEPERIDINE OR LEVODOPA INCREASES INCIDENCE OF ADVERSE EFFECTS.

NAFCILLIN (UNIPEN) PLASMA LEVELS ARE INCREASED BY CONCOMITANT USE OF PROBENECID (BENEMID).

NEOMYCIN IN COMBINATION WITH OTHER AMINOGLYCOSIDE ANTIBIOTICS INCREASES INCIDENCE OF OTOTOXICITY AND NEPHROTOXICITY. CONCOMITANT USE WITH ETHACRYNIC ACID POTENTIATES THE OTOTOXICITY. IT POTENTIATES NEUROMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS. WHEN ADMINISTERED BY THE ORAL ROUTE IT MAY INCREASE THE ACTIVITY OF ORAL ANTICOAGULANTS.

NITROGLYCERIN MAY PRODUCE HYPOTENSION FOLLOWING COMBINED USE WITH ETHYL ALCOHOL. CHRONIC ADMINISTRATION OF PENTAERYTHRITOL TETRANITRATE (PERITRATE) MAY PRODUCE A TOLERANCE TO NITROGLYCERIN.

ORPHENADRINE (NORFLEX) IN COMBINATION WITH PROPOXYPHENE (DARVON) MAY PRODUCE MENTAL CONFUSION AND ANXIETY.

OXYPHENBUTAZONE (TANDEARIL) ELEVATES THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS. OXYPHENBUTAZONE PLASMA LEVELS MAY BE ELEVATED BY ANABOLIC STEROIDS.

PENICILLIN G AND DERIVATIVES-PLASMA LEVELS ARE ELEVATED BY PROBENECID (BENEMID) AND SALICYLATES.

PENTAERYTHRITOL TETRANITRATE (PERITRATE) THERAPY MAY PRODUCE A TOLERANCE TO NITROGLYCERIN.

PHENOTHIAZINES MAY ANTAGONIZE LEVODOPA AND THE CENTRAL EFFECTS OF AMPHETAMINES. ADDITIVE EFFECTS OCCUR WITH CONCOMITANT USE OF OTHER CNS DEPRESSANTS AND ANTIHISTAMINES. ADDITIVE CARDIAC DEPRESSANT EFFECTS ARE POSSIBLE WITH QUINIDINE. PROCARBAZINE (MATULANE) MAY POTENTIATE THE CNS DEPRESSANT EFFECTS OF PHENOTHIAZINES.

PHENYLBUTAZONE (BUTAZOLIDIN) ELEVATES THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS AND POTENTIATES THE HYPOGLYCEMIC RESPONSE TO SULFONYLUREAS. PHENYLBUTAZONE PLASMA LEVELS MAY BE ELEVATED BY ANABOLIC STEROIDS.

PHENYLEPHRINE ADMINISTERED NASALLY OR SYSTEMICALLY MAY BE POTENTIATED BY GUANETHIDINE (ISMELIN) AND MAOI.

PHENYLPROPANOLAMINE MAY BE POTENTIATED BY MAOI.

PHENYRAMICOL (ANALEXIN) ELEVATES THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS AND POTENTIATES THE ACTIVITY OF DIPHENYLHYDANTOIN AND SULFONYLUREAS.

POLYMYXIN B (AEROSPORIN) ENHANCES NEUROMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS. IN COMBINATION WITH OTHER AMINOGLYCOSIDE ANTIBIOTICS IT INCREASES INCIDENCE OF OTOTOXICITY AND NEPHROTOXICITY.

PROBENECID (BENEMID) ELEVATES PLASMA LEVELS OF AMINOSALICYLIC ACID, DAPSONE (AVLCSULFON), CEPHALOSPORINS, PENICILLIN G AND DERIVATIVES AND INDOMETHACIN. SALICYLATES INHIBIT URICOSURIC ACTIVITY OF PROBENECID.

PROCAINAMIDE (PRONESTYL) - ADDITIVE HYPOTENSIVE EFFECTS MAY OCCUR WITH CONCOMITANT USE OF ANTIHYPERTENSIVE AGENTS.

PROCARBAZINE (MATULANE) MAY POTENTIATE THE EFFECTS OF PHENOTHIAZINES AND CNS DEPRESSANTS. IT MAY PRODUCE ADDITIVE HYPOTENSIVE EFFECTS WITH GUANETHIDINE (ISMELIN).

PROPOXYPHENE (DARVON) IN COMBINATION WITH ORPHENADRINE (NORFLEX) MAY PRODUCE MENTAL CONFUSION AND ANXIETY.

PROPRANOLOL (INDERAL) MAY POTENTIATE ORAL HYPOLYCEMICS AND ANTI-HYPERTENSIVES. IT ANTAGONIZES PHARMACOLOGICAL ACTIONS OF SYMPATHOMIMETICS. PROPRANOLOL-INDUCED ADVERSE EFFECTS ARE ANTAGONIZED BY ANTICHOLINERGICS. ADDITIVE CARDIAC DEPRESSANT EFFECTS ARE POSSIBLE WITH QUINIDINE AND PHENOTHIAZINES.

PYRIDOXINE (VITAMIN B6) ANTAGONIZES THE PHARMACOLOGICAL EFFECTS OF LEVODOPA.

QUINIDINE MAY POTENTIATE GUANETHIDINE, ORAL ANTICOAGULANTS AND THE NEUROMUSCULAR BLOCKADE OF MUSCLE RELAXANTS. IT MAY BE POTENTIATED BY ANTI-CHOLINERGICS. ACETAZOLAMIDE (DIAMOX), SODIUM BICARBONATE AND THIAZIDE DIURETICS INCREASE RENAL REABSORPTION. ADDITIVE CARDIAC DEPRESSANT EFFECTS ARE POSSIBLE WITH PROPRANOLOL.

RESERPINE IS POTENTIATED BY METHOTRIMEPRAZINE (LEVOPROME). IT MAY ANTAGONIZE THE EFFECTS OF LEVODOPA.

SALICYLATES ELEVATE THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS, INCREASE PLASMA LEVELS OF UNBOUND PENICILLIN G AND DERIVATIVES AND POTENTIATE METHOTREXATE AND SULFONYLUREAS. SALICYLATE PLASMA LEVELS MAY BE DECREASED BY CORTICOSTEROIDS. THEY MAY DECREASE SERUM LEVELS OF INDOMETHACIN (INDOCIN) AND INHIBIT URICOSURIC ACTIVITY OF SULFINPYRAZONE (ANTURANE) AND PROBENECID (BENEMID).

SURGICAL SKELETAL MUSCLE RELAXANTS ARE POTENTIATED BY AMINOGLYCOSIDE ANTIBIOTICS, AMPHOTERICIN B, FUROSEMIDE, MAGNESIUM IONS, METHOTRIMEPRAZINE (LEVOPROME), QUINIDINE AND THIAZIDE DIURETICS. ECHOTHIOPHATE IODIDE POTENTIATES THE EFFECTS OF SUCCINYLCHOLINE.

SMALL POX VACCINATION MAY RESULT IN GENERALIZED VACCINA WITH CONCOMITANT USE OF METHOTREXATE.

SODIUM BICARBONATE ELEVATES SERUM LEVELS OF AMPHETAMINES, TRICYCLIC ANTIDEPRESSANTS AND QUINIDINE BY ENHANCING RENAL REABSORPTION. IT MAY ANTAGONIZE METHENAMINE COMPOUNDS AND LITHIUM CARBONATE AND DECREASE ORAL ABSORPTION OF TETRACYCLINES.

SODIUM CHLORIDE IN LARGE DOSES MAY ANTAGONIZE PHARMACOLOGICAL EFFECTS OF LITHIUM CARBONATE. LOW SODIUM INTAKE MAY PRECIPITATE LITHIUM TOXICITY.

SODIUM POLYSTYRENE SULFONATE RESIN (KAYEXALATE) BINDS MAGNESIUM AND CALCIUM IONS FOUND IN ANTACIDS RESULTING IN SYSTEMIC ALKALOSIS.

STREPTOMYCIN IN COMBINATION WITH AMINOGLYCOSIDE ANTIBIOTICS INCREASES INCIDENCE OF OTOTOXICITY AND NEPHROTOXICITY. ETHACRYNIC ACID POTENTIATES THE OTOTOXICITY. IT POTENTIATES NEUROMUSCULAR BLOCKADE OF SKELETAL MUSCLE RELAXANTS.

SULFINPYRAZONE (ANTURANE) INDUCED URICOSURIA IS INHIBITED BY SALICYLATES.

SULFONAMIDES MAY POTENTIATE THE HYPOGLYCEMIC RESPONSE TO ORAL HYPOGLYCEMICS AND ELEVATE SERUM LEVELS OF METHOTREXATE. CONCOMITANT USE WITH METHENAMINE COMPOUNDS FREQUENTLY RESULTS IN CRYSTALLURIA AND THE FORMATION OF A PRECIPITATE.

TETRACYCLINE ABSORPTION IS DECREASED BY ANTACIDS CONTAINING DIVALENT OR TRIVALENT CATIONS, SODIUM BICARBONATE AND IRON SALTS. IT MAY ELEVATE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS AND POTENTIATE NEPHROTOXIC EFFECTS OF METHOXYFLURANE (PENTHRANE).

THIAZIDE DIURETICS MAY PRECIPITATE DIGITALIS TOXICITY AND ANTAGONIZE THE EFFECTS OF HYPOGLYCEMICS. NEUROMUSCULAR BLOCKADE PRODUCED BY SURGICAL MUSCLE RELAXANTS MAY BE ENHANCED. CONCOMITANT USE WITH CORTICOSTEROIDS MAY RESULT IN EXCESSIVE POTASSIUM LOSS. THEY MAY PRODUCE ADDITIVE HYPOTENSIVE EFFECTS WITH GUANETHIDINE (ISMELIN) AND METHYLDOPA (ALDOMET).

THYROID PREPARATIONS MAY POTENTIATE THE ANTICOAGULANT RESPONSE TO ORAL ANTICOAGULANTS. CHOLESTYRAMINE DECREASES ABSORPTION BY BINDING THYROXINE AND TRIIODOTHYRONINE. THEY MAY DECREASE ACTIVITY OF HYPOGLYCEMIC AGENTS.

APPENDIX VI

Computer Program

LINE NO.	SEQ. NO.	SOURCE STATEMENT	CBD CL3-7 03/20/72
1	001010	IDENTIFICATION DIVISION.	
2	001020	PROGRAM-TC. 'CDIRPT'.	
3	001030	AUTHOR: P E PLATIAU & G D MAHONEY.	
4	001040	REMARKS. SAMPLE PROGRAM FOR RETRIEVAL OF DRUG-DRUG INTERACTION	
5	001050	SUMMARIES WITH SAMPLE PROFILE.	
6	001060	ENVIRONMENT DIVISION.	
7	001070	CONFIGURATION SECTION.	
8	001080	SOURCE-COMPUTER. IBM-360 E30.	
9	001090	OBJECT-COMPUTER. IBM-360 E30.	
10	001100	INPUT-OUTPUT SECTION.	
11	001110	FILE-CONTROL.	
12	001120	SELECT CARD ASSIGN TO 'SYS004' UNIT-RECORD 2540R.	
13	001130	SELECT PRINT ASSIGN TO 'SYS005' UNIT-RECORD 1403.	
14	001140	SELECT DISK ASSIGN TO 'SYS013' DIRECT-ACCESS 2314	
15	001150	ACCESS IS RANDOM, ORGANIZATION IS INDEXED,	
16	001160	RESERVE NO ALTERNATE AREA, SYMBOLIC KEY IS REC-ID,	
17	001170	RECORD KEY IS DSK-NO.	
18	002010	DATA DIVISION.	
19	002020	FILE SECTION.	
20	002030	FC CARD	
21	002040	RECORD CONTAINS 30 CHARACTERS, LABEL RECORD IS OMITTED,	
22	002050	DATA RECORD IS CD, RECORDING MODE IS F.	
23	002060	01 CD.	
24	002061	02 CD-IN PICTURE X(79).	
25	002062	02 CODE PICTURE X.	
26	002063	88 HED VALUE 'A'.	
27	002064	88 MED VALUE 'B'.	
28	002065	88 DAT VALUE 'C'.	
29	002070	FC PRINT	
30	002080	RECORD CONTAINS 133 CHARACTERS, LABEL RECORD IS OMITTED,	
31	002090	DATA RECORD IS PRT, RECORDING MODE IS F.	
32	002100	01 PRT PICTURE X(133).	
33	002110	FC DISK	
34	002120	RECORD CONTAINS 671 CHARACTERS, LABEL RECORD IS STANDARD,	
35	002130	DATA RECORD IS DSK, RECORDING MODE IS F.	
36	002140	01 DSK.	
37	002150	02 DSK-NO PICTURE X(5).	
38	002160	02 MSG, OCCURS 9 TIMES.	
39	002170	03 DSK-MSG PICTURE X(74).	
40	003010	WORKING-STORAGE SECTION.	
41	003020	77 A PICTURE S9999 COMPUTATIONAL VALUE 0.	
42	003030	77 B PICTURE S9999 COMPUTATIONAL VALUE 0.	
43	003040	77 C PICTURE S9999 COMPUTATIONAL VALUE 0.	
44	003050	77 RDSW PICTURE 99 COMPUTATIONAL-3 VALUE 1.	
45	003060	77 LIN-CNT PICTURE 99 COMPUTATIONAL-3 VALUE 0.	
46	003070	77 CC PICTURE X.	
47	003080	77 PAG-CNT PICTURE 99 COMPUTATIONAL-3 VALUE 0.	
48	003090	77 NAME-STOR PICTURE X(21).	
49	003100	77 PT-NO-STOR PICTURE 9(7) COMPUTATIONAL-3 VALUE 0.	
50	003110	77 PT-RM-STOR PICTURE XXX.	
51	003120	77 REC-ID PICTURE X(5).	
52	003125	77 DAY-STOR PICTURE XX.	
53	003130	01 TABLE.	
54	003140	02 LINE, OCCURS 30 TIMES.	

LINE NO.	SEQ. NO.	SOURCE STATEMENT
55	003150	03 TBL-NO PICTURE X(5).
56	003160 01	HOSP-HED.
57	003170	02 FILLER PICTURE X(29) VALUE SPACES.
58	003180	02 TITLE PICTURE X(22).
59	003190	02 FILLER PICTURE X(82) VALUE SPACES.
60	004010 01	PT-HED.
61	004020	02 FILLER PICTURE X(12) VALUE SPACES.
62	004030	02 FILLER PICTURE X(35) VALUE
63	004040	'CUMULATIVE MEDICATION PROFILE FOR '.
64	004050	02 PRT-NAM PICTURE X(21).
65	004060	02 FILLER PICTURE X(65) VALUE SPACES.
66	004070 01	UNDERLIN1.
67	004080	02 FILLER PICTURE X(47) VALUE SPACES.
68	004090	02 FILLER PICTURE X(21) VALUE ALL '-'. .
69	004100	02 FILLER PICTURE X(65) VALUE SPACES.
70	004110 01	PT-HED1.
71	004120	02 FILLER PICTURE X(12) VALUE SPACES.
72	004130	02 FILLER PICTURE X(4) VALUE 'NO. '.
73	004140	02 PT-NO-PRT PICTURE 9(7).
74	004150	02 FILLER PICTURE X(16) VALUE ' ROOM '.
75	004160	02 PT-RM-PRT PICTURE XXX.
76	004170	02 FILLER PICTURE X(16) VALUE ' AGE '.
77	004180	02 PT-AG-PRT PICTURE 99.
78	004190	02 FILLER PICTURE X(64) VALUE SPACES.
79	005010 01	COL-HED.
80	005020	02 FILLER PICTURE X(80) VALUE
81	005030	' START STOP MEDICATION ORDERED
82	005040	' PHYSICIAN
83	005050	02 FILLER PICTURE X(53) VALUE SPACES.
84	005060 01	UNDERLIN2.
85	005070	02 FILLER PICTURE X(80) VALUE
86	005080	'
87	005090	'
88	005100	02 FILLER PICTURE X(53) VALUE SPACES.
89	005110 01	PRT-LIN.
90	005120	02 FILLER PICTURE XXX VALUE SPACES.
91	005130	02 MTH-IN1 PICTURE XX.
92	005140	02 FILLER PICTURE X VALUE ' / '.
93	005150	02 DAY-IN1 PICTURE XX.
94	005160	02 FILLER PICTURE XX VALUE SPACES.
95	005170	02 MTH-OUT1 PICTURE XX.
96	005180	02 SLASH PICTURE X.
97	005190	02 DAY-OUT1 PICTURE XX.
98	005200	02 FILLER PICTURE XX VALUE SPACES.
99	005210	02 PRT-ORD PICTURE X(46).
100	005220	02 FILLER PICTURE XX VALUE SPACES.
101	005230	02 PRT-MD PICTURE X(12).
102	005240	02 FILLER PICTURE X(56) VALUE SPACES.
103	006010 01	PT-HED2.
104	006020	02 FILLER PICTURE XXX VALUE SPACES.
105	006030	02 PRT-NAM2 PICTURE X(21).
106	006040	02 FILLER PICTURE X(8) VALUE ' NO. '.
107	006050	02 PT-NO-PRT2 PICTURE 9(7).
108	006060	02 FILLER PICTURE X(17) VALUE ' ROOM '.

LINE NO.	SEQ. NO.	SOURCE STATEMENT
109	006070	02 PT-RM-PRT2 PICTURE XXX.
110	006080	02 FILLER PICTURE X(12) VALUE ' PAGE '.
111	006090	02 PAGE-NO PICTURE ZZ9.
112	006100	02 FILLER PICTURE X(59) VALUE SPACES.
113	006110 01	PT-HE03.
114	006120	02 FILLER PICTURE X(41) VALUE
115	006130	' PROBABLE DRUG-DRUG INTERACTIONS FOR '.
116	006140	02 PRT-NAM3 PICTURE X(21).
117	006150	02 FILLER PICTURE X(5) VALUE ' NO. '.
118	006160	02 PT-NO-PRT3 PICTURE 9(7).
119	006170	02 FILLER PICTURE X(59) VALUE SPACES.
120	007010 01	MESSG.
121	007020	02 FILLER PICTURE XXX VALUE SPACES.
122	007030	02 PRT-MSG PICTURE X(74).
123	007040	02 FILLER PICTURE X(56) VALUE SPACES.
124	007050 01	TEL-HE0.
125	007060	02 FILLER PICTURE X(80) VALUE
126	007070	' FOR FURTHER INFORMATION CALL DRUG INFORMATION CENTER E
127	007080	'XT 1234
128	007090	02 FILLER PICTURE X(53) VALUE SPACES.
129	007100 01	DATE-HE0.
130	007110	02 FILLER PICTURE X(29) VALUE SPACES.
131	007120	02 FILLER PICTURE X(15) VALUE 'END OF PROFILE '.
132	007130	02 DATE-STOR PICTURE X(8).
133	007140	02 FILLER PICTURE X(52) VALUE SPACES.
134	008010 01	CD-AREA.
135	008020	02 PT-DATA.
136	008030	03 PT-NAM PICTURE X(21).
137	008035	03 PT-NO PICTURE 9(7).
138	008040	03 PT-RM PICTURE XXX.
139	008050	03 PT-AGE PICTURE 99.
140	008060	03 FILLER PICTURE X(46).
141	008070	02 MED-DATA REDEFINES PT-DATA.
142	008080	03 MED-CRD PICTURE X(46).
143	008090	03 MSG-NO PICTURE X(5).
144	008100	03 DAT-IN.
145	008110	04 MTH-IN PICTURE XX.
146	008120	04 DAY-IN PICTURE XX.
147	008130	03 DAT-CUT.
148	008140	04 MTH-OUT PICTURE XX.
149	008150	04 DAY-CUT PICTURE XX.
150	008160	03 MD PICTURE X(12).
151	008170	03 FILLER PICTURE X(8).
152	008180	02 DAT-DATA REDEFINES MED-DATA.
153	008190	03 DATE.
154	008200	04 MTH PICTURE XX.
155	008210	04 FILLER PICTURE X.
156	008220	04 DAY PICTURE XX.
157	008230	04 FILLER PICTURE X.
158	008240	04 YR PICTURE XX.
159	008250	03 FILLER PICTURE X(71).
160	009010	PROCEDURE DIVISION.
161	009020	START.
162	009025	PERFORM TBL-BLNK VARYING A FROM 1 BY 1 UNTIL A, 30.

LINE NO.	SEQ. NO.	SOURCE STATEMENT
163	009030	OPEN INPUT CARD DISK OUTPUT PRINT.
164	009040	CORD.
165	009050	READ CARD AT END GO TO EOJ.
166	009055	MOVE CD-IN TO CD-AREA.
167	009056	IF DAT GO TO DATE-SAV.
168	009060	IF RDSW = 1 GO TO FIRST-RTN.
169	009070	IF HED GO TO SUMRY.
170	009080	PROFILE.
171	009090	IF LIN-CNT , 26 PERFORM HED-RTN2.
172	009095	MOVE MTH-IN TO MTH-IN1. MOVE DAY-IN TO DAY-IN1.
173	009100	MOVE MED-CRD TO PRT-CRD. MOVE MD TO PRT-MD.
174	009105	IF DAY-OUT = ' ' MOVE ' ' TO SLASH ELSE MOVE '/' TO SLASH.
175	009110	MOVE MTH-CUT TO MTH-OUT1. MOVE DAY-CUT TO DAY-OUT1.
176	009115	PERFORM RITE-LINE. IF DAY-OUT = ' ' GO TO CHK-RTN.
177	009120	IF DAY-OUT / DAY-STOR GO TO CORD ELSE GO TO CHK-RTN.
178	009130	RITE-LINE.
179	009135	MOVE PRT-LIN TO PRT. PERFORM RITE-RTN. ADD 1 TO LIN-CNT.
180	009140	CHK-RTN.
181	009150	IF MSG-NO = ' ' GO TO CORD.
182	009160	PERFORM MSG-CHK VARYING A FROM 1 BY 1 UNTIL TBL-NO (A) = ' '.
183	009180	MOVE MSG-NO TO TBL-NO (A). GO TO CORD.
184	010010	FIRST-RTN.
185	010020	IF MED GO TO CORD. MOVE 0 TO RDSW.
186	010030	PERFORM HED-RTN1. GO TO CORD.
187	010040	HED-RTN1.
188	010050	MOVE 1 TO CC. MOVE ' ' MODERN HOSPITAL ' ' TO TITLE.
189	010060	MOVE HOSP-HED TO PRT. PERFORM RITE-RTN. MOVE 0 TO CC.
190	010070	MOVE 'DEPARTMENT OF PHARMACY' TO TITLE. MOVE HOSP-HED TO PRT.
191	010080	PERFORM RITE-RTN. MOVE PT-NAM TO PRT-NAM NAME-STOR.
192	010090	MOVE PT-HED TO PRT. PERFORM RITE-RTN. MOVE ' ' TO CC.
193	010100	MOVE UNDERLIN1 TO PRT. PERFORM RITE-RTN. MOVE 0 TO CC.
194	010110	MOVE PT-NC TO PT-NO-STOR PT-NO-PRT.
195	010120	MOVE PT-RM TO PT-RM-STOR PT-RM-PRT.
196	010130	MOVE PT-AGE TO PT-AG-PRT.
197	010140	MOVE PT-HED1 TO PRT. PERFORM RITE-RTN.
198	010150	MOVE COL-HED TO PRT. PERFORM RITE-RTN. MOVE ' ' TO CC.
199	010160	MOVE UNDERLIN2 TO PRT. PERFORM RITE-RTN.
200	010170	MOVE 0 TO CC, A, B.
201	010175	MOVE 5 TO LIN-CNT. MOVE 1 TO PAG-CNT.
202	011010	HED-RTN2.
203	011015	MOVE 'CONTINUED ON NEXT PAGE' TO TITLE. MOVE HOSP-HED TO PRT.
204	011016	PERFORM RITE-RTN.
205	011020	MOVE 1 TO CC. MOVE 0 TO LIN-CNT.
206	011030	MOVE NAME-STOR TO PRT-NAM2.
207	011040	MOVE PT-NC-STOR TO PT-NO-PRT2.
208	011050	MOVE PT-RM-STOR TO PT-RM-PRT2.
209	011060	ADD 1 TO PAG-CNT. MOVE PAG-CNT TO PAGE-NO.
210	011070	MOVE PT-HED2 TO PRT. PERFORM RITE-RTN. MOVE 0 TO CC.
211	011080	HED-RTN3.
212	011090	MOVE 1 TO CC. MOVE 0 TO LIN-CNT.
213	011100	MOVE NAME-STOR TO PRT-NAM3.
214	011110	MOVE PT-NC-STOR TO PT-NO-PRT3.
215	011120	MOVE PT-HED3 TO PRT. PERFORM RITE-RTN.
216	011130	DATE-SAV.

LINE NO.	SEQ. NO.	SOURCE STATEMENT
217	011140	MOVE DATE TO DATE-STCR. MOVE DAY TO DAY-STOR. GO TO CORD.
218	012010	SUMRY.
219	012020	MOVE DATE-HED TO PRT. PERFORM RITE-RTN.
220	012040	SUMRY1.
221	012050	PERFORM HED-RTN3.
222	012060	SLMRY-RITE.
223	012070	ADD 1 TO B. IF TBL-NO (B) = ' ' GO TO END-RPT.
224	012080	MOVE TBL-NO (B) TO REC-ID. MOVE 0 TO CC.
225	012090	READ DISK INVALID KEY GO TO SUMRY-RITE.
226	012100	PERFORM DSK-RITE VARYING C FROM 1 BY 1 UNTIL DSK-MSG (C) =
227	012110	' '. ADD 1 TO LIN-CNT.
228	012120	IF LIN-CNT = 26 GO TO SUMRY1 ELSE GO TO SUMRY-RITE.
229	012130	END-RPT.
230	012140	MOVE TEL-HED TO PRT. MOVE ' ' TO CC.
231	012150	PERFORM RITE-RTN. IF RDSW = 3 GO TO CLOSE1.
232	012160	PERFORM TBL-PLNK VARYING A FROM 1 BY 1 UNTIL A = 30.
233	012170	PERFORM HEC-RTN1. GO TO CORD.
234	013010	DSK-RITE.
235	013020	MOVE DSK-MSG (C) TO PRT-MSG.
236	013030	MOVE MESSG TO PRT. PERFORM RITE-RTN.
237	013040	MOVE ' ' TO CC. ADD 1 TO LIN-CNT.
238	013050	TBL-BLNK.
239	013060	MOVE ' ' TO TBL-NO (A).
240	013070	MSG-CHK.
241	013080	IF MSG-NO = TBL-NO (A) GO TO CORD.
242	013090	RITE-RTN.
243	013100	WRITE PRT AFTER ADVANCING CC LINES.
244	013110	EOJ.
245	013120	MOVE 3 TO RDSW. GO TO SUMRY.
246	013130	CLOSE1.
247	013150	CLOSE CARD PRINT DISK.
248	013160	STOP RUN.