PROVISION AND USE OF DRUG INFORMATION

by

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PROVISION AND USE OF DRUG INFORMATION

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INTRODUCTION

Information about drugs and drug therapy is available from many different sources, with various interests in influencing the prescribing habits of doctors. Although drug information sources are plentiful, this does not necessarily mean that all the information required by the prescribing doctor is readily available in a compact source.

The aim of this study was to examine the ways in which doctors obtain information about drugs, and to study the information provided by the major existing sources, to establish their ability to fulfill the information needs of doctors. For the purposes of this study, drug information was defined as knowledge of facts or opinions acquired by reading, study or practical experience concerning any chemical substance which is intended for use in diagnosis, prevention, treatment or cure of disease, or to enhance the physical or mental well being of an individual.

In chapter one, the ways in which the government has itself provided and influenced the provision of information by other bodies are discussed. Since the nationalisation of the health service in 1948, the government has been concerned about the size of the nation's drug bill. It attempted to reduce this cost and to promote rational prescribing by providing information about drugs to the medical profession. More recently, it has dropped this advisory role, and has concentrated on ensuring that information provided by others is of a sufficiently high standard.

Two studies of the use of drug information by general

practitioners have already been made.[1,2] Both indicated that general practitioners regard recommendations from consultants as a valuable source of information. Therefore, a study of the use of drug information sources by hospital doctors was carried out. Two other factors influenced this choice of a hospital environment. Firstly, hospital doctors often require more specific and extensive drug information than is needed by their general practitioner colleagues. Secondly, hospital doctors usually have easier access to medical libraries and, more recently, drug information services provided by information pharmacists, than general practitioners. The results of the survey are described in chapter two.

The majority of hospital doctors use reports of clinical trials published in journals as a source of information about new drugs. The analysis of the information contained in a sample of clinical trial reports appearing in several major British medical journals is reported in chapter three.

Many of the hospital doctors indicated that promotional material was an important source of information, particularly for learning about the existence of new drugs. Several studies of the provision of drug information by medical representatives, direct mail and journal advertisements have been made and these are critically reviewed in chapter four. The majority of drug firms are members of the Association of the British Pharmaceutical Industry (ABPI). The ABPI issues a code of practice and adherance to this code is a condition of membership of the Association. The code requires that certain information must be provided in drug advertisements, in addition to the legal requirements. A comparison between

the information that the prescribing doctor requires and the information that is provided in advertisements is made in the chapter four.

Most of the hospital doctors stated that they had written to a pharmaceutical firm for further information about a drug, at some stage in their medical career. A survey was carried out to discover how medical information staff in the pharmaceutical industry provide information about their own company's products to members of the medical profession. The results of this study are described in chapter five.

It was not possible to study the provision of information about drugs without being aware of two areas of current controversy. Firstly, the medical profession, the government and the pharmaceutical industry have all expressed concern about the reporting of adverse reactions to drugs. This is in the wake of the "practolol" disaster, which occurred despite the strict legislation affecting drug safety being operative. There is currently much debate about new and improved methods of monitoring the use of drugs for adverse reactions. The methods currently in use, and proposed methods are reviewed in Appendix E of the last chapter. Secondly, a relatively new development in drug information services has been the establishment of drug information centres, which are manned by information pharmacists. Although they attempt to provide a fully comprehensive drug information service, it appears that they are used by few medical staff. The literature concerning their development and use is reviewed in Appendix F of the last chapter. In addition, the experience of British drug information centres is compared

with the experience of centres in the U.S., where they have been in existence since 1962.

Since the majority of the data collected during this study were not normally distributed, non-parametric methods of analysis have been used to test significant differences between various groups of data. The chi-squared and the Wilcoxon matched-pairs signed-ranks tests have been used for this purpose.

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CHAPTER 1

THE GOVERNMENT'S INFLUENCE ON THE PROVISION OF DRUG INFORMATION TO MEDICAL DOCTORS

Ever since the nationalisation of the health service in 1948, the government has tried to ensure that it is not being exploited by the drug manufacturers. The main areas of concern have been with the provision of drug information to prescribing doctors and the safety and cost of pharmaceutical products. Control of safety and cost has indirectly affected the provision of drug information.

Legislation governing Drug Information

The Medicines Act of 1968 controls two types of drug information - advertisements and data sheets. The manufacturer is prevented from promoting a product unless a data sheet relating to the product has been provided to all prescribing doctors, in the fifteen months before the promotional campaign begins.

The purpose of a data sheet is to provide the essential particulars about the medicinal product in a convenient form for reference. Data sheets are of a fixed size, colour and typography and therefore are not considered to be advertisements. They must contain the following information:

1. the brand and approved name;
2. the presentation - including a description of the appearance of the product;
3. the uses - including the product's main pharmacological actions and indications;

4. the dosage and method of administration;
5. contra-indications, warnings, precautions, overdosage treatment, main side effects and adverse reactions associated with the product;
6. pharmaceutical precautions including storage instructions;
7. the legal category;
8. the package quantities;
9. further information which will assist in the proper understanding, recognition, administration and use of the product;
10. product licence numbers, names and addresses of manufacturers;
11. date of preparation or last review.

The Association of the British Pharmaceutical Industry (ABPI) publishes an annual compendium which contains data sheets provided by the firms that are members of the association. This compendium is distributed free of charge to prescribing doctors.

Regulations relating to advertisements state that any commercially interested party who issues a false or misleading advertisement, relating to medicinal products, is guilty of an offence. Only the uses specified in the product licence are allowed to be recommended. In addition, no advertisement may state or imply that the product has been approved by the Committee on Safety of Medicines.

The legal requirements relating to the provision of drug information have succeeded in ensuring that each prescribing doctor obtains an objective statement about each promoted product and that any form of advertising does

not convey false or misleading information.

The Safety of Pharmaceutical Products

Until 1964 there was no requirement for a manufacturer to seek the approval of an independent body to test a new product, or to launch products on to the market. The demand for control of these two stages followed the thalidomide disaster. It was answered by the setting up of the Committee on Safety of Drugs, whose original terms of reference were to review the available evidence for new drugs and to advise on their toxicity. The committee had no legal powers and operated on a voluntary basis. The major pharmaceutical companies agreed to obtain the approval of the committee before initiating a clinical trial with a new drug and also before placing it on the market. A clinical trial is defined as an investigation which involves the administration of medicinal products, where there is evidence that they may be beneficial to patients, to ascertain what effects, beneficial or harmful, the products have.

The voluntary system was replaced by comprehensive legislation in the Medicines Act of 1968, which was implemented in September 1971. The Act controls manufacturing, importation, sale and supply, labelling and advertising of medicines. A Medicines Commission was established to advise on the enforcement of the Act and also to function as an appeal body in respect of the activities of a number of expert advisory committees. The expert committee dealing with the clinical trials and marketing is the Committee on Safety of Medicines (CSM), which replaced the Committee on Safety of Drugs.

The CSM is itself served by expert sub-committees advising on the issuing of licences and certificates. The Licensing Authority issues Clinical Trial Certificates which are valid for two years for drugs approved by the CSM and Product Licences valid for five years for drugs approved for marketing.

The Licensing Authority does not lay down rigid requirements concerning the data that must be provided before a Clinical Trial Certificate can be issued. The Department of Health and Social Security (DHSS) does prepare guidelines for applicants. Each application should include details of:

1. the clinical trial protocol. This should state the number of patients, the indications for which they are treated, the maximum daily dosage to be employed and the duration of the drug treatment. Details of the trial design and safety monitoring are also expected;
2. the pharmaceutical aspects of the formulation. The purity, stability and the characteristics of the product's release from the final formulation will be considered;
3. experimental studies in animals and man. These should show sufficient promise of therapeutic potential to justify the study. Pharmacological studies should demonstrate the full mode of action of a drug by the proposed method of administration in the trial. Pharmacokinetic data are expected to provide information on the probable method of absorption, distribution and excretion of the drug in man. Toxicological data are required to demonstrate the pattern of toxicity. The effects of sub-acute (therapeutic) and chronic (above therapeutic) dosage in at least two species of animals

are usually reported. Reproduction studies are required to assess the effects of the drug on the foetus, neonate, mother and the fertility of adults in two species of animals, including a rodent. Possible carcinogenic effects of drugs are also required to be studied. Details of any human pharmacological studies in volunteers should be reported if they have any relevance to the drug's safety. Studies in man are not mandatory because it may be unethical to carry out such studies. Any clinical studies performed outside the U.K. which are relevant to the application should be included.

Providing the data are considered to be satisfactory, the CSM will advise the Licensing Authority to issue a Clinical Trial Certificate. The holder of the certificate is obliged to inform the Licensing Authority of any serious or unexpected adverse reactions which occur in the course of the trial.

An application for a Product Licence normally contains details of the product including chemical, pharmaceutical and pharmacological data, data from experimental and biological studies in man and animals and evidence of the product's safety and efficacy in patients. Information provided in an application for a Clinical Trial Certificate and a Product Licence are therefore partly overlapping.

When the licensing began in 1971, the Medicines Act made a provision for medicinal products already on the market on the first of September 1971, to be granted a Product Licence of Right. These licences were granted automatically without the products' safety, efficacy and quality being considered. Valid applications were received for about 55,000 products by

the closing date on the 1st July 1972.[1] The Committee on the Review of Medicines was established in 1975 to scrutinise these products.

Information on safety, efficacy and quality is requested from the licence holders and this is considered by the committee, together with any other relevant information. On this basis,the committee makes recommendations as to the permitted indications for use, contraindications and warnings of the products. During its first year of operation, 10,000 products were withdrawn from the market,[2] and recently the committee's recommendations concerning non-steroid anti-inflammatory agents were published.[3]

These new safety measures have increased the amount of drug information available to the prescribing doctor. Firstly, an increasing number of reports of clinical trials have been published in medical journals since 1960 (see Chapter 3). Manufacturers are usually able to provide copies of the published reports which concern their own products, to doctors who do not have easy access to libraries.[4] Secondly, the majority of pharmaceutical firms are willing to provide unpublished drug information to members of the medical profession (see Chapter 5),if this information is needed to answer an enquiry.

The CSM does not publish or circulate any drug information obtained from a submission for a Clinical Trial Certificate or a Product Licence. However, the Committee on the Review of Medicines does provide drug information in the publication of its recommendations concerning products that obtained Licences of Right.

The necessity for a manufacturer to obtain permission from a

regulatory body before testing and marketing a new product would have probably have prevented the thalidomide disaster. Unfortunately, the recent disaster involving practolol (Eraldin) indicated that these measures alone are not sufficient. Practolol was found to cause a serious and unexpected adverse reaction, which was only detected after four years of marketing. In the U.K. adverse reactions to drugs are reported to the CSM on a voluntary basis. The CSM is currently concerned about the failure of this system to detect the reaction caused by practolol and the low rate of reporting by medical practitioners.[2] Recently the data sheet and the Monthly Index of Medical Specialities (MIMS)which is a drug information handbook have identified all newly introduced products with an inverted triangle symbol (▼). The CSM requests doctors to make a special effort in the reporting of any adverse reactions associated with these products. (Full details of the current debate concerning alternative methods of reporting adverse reactions appears in Chapter 5, Appendix5E). It appears unlikely that legislation will be used to force doctors to report any untoward event occurring while a patient is taking a drug.

The CSM actively disseminate the information they receive about adverse reactions in three types of publication:

1. Register of Adverse Reactions which lists the reported adverse drug reactions associated with particular products;
2. Adverse Reactions Leaflets which are used for urgent warnings and dangerous adverse reactions;
3. Current Problems Leaflets which discuss topics that

are not sufficiently defined to warrant the issue of a warning in the Adverse Reactions Leaflets series.

The Register of Adverse Reactions is sent to all hospital chief pharmacists and all schools of pharmacology and therapeutics. Both types of leaflet are distributed to all members of the medical profession.

The Cost of Pharmaceutical Products

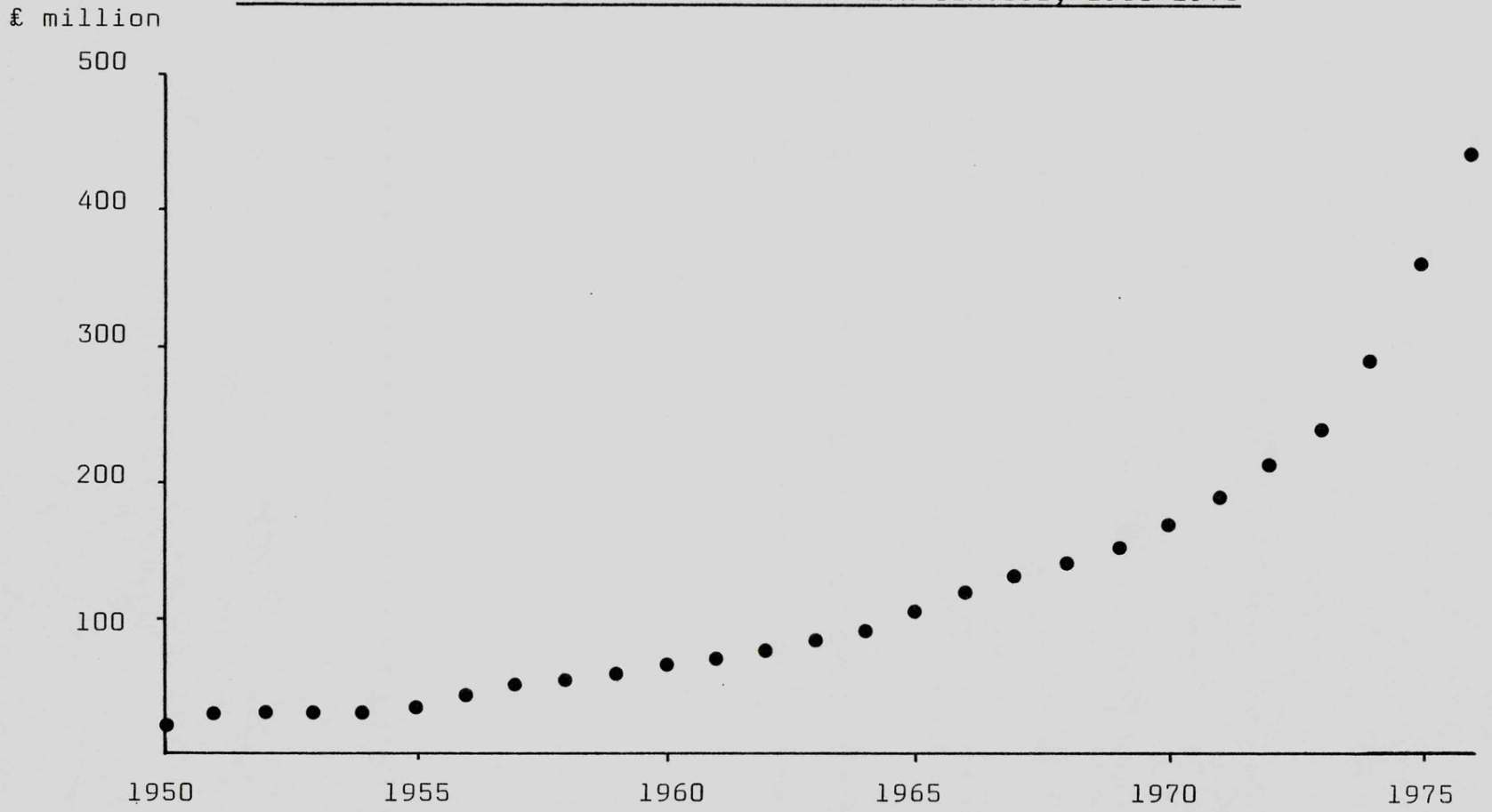
The government has attempted to reduce the cost of drugs to the National Health Service (NHS) in several different ways. Firstly, the prices and profits of the manufacturers have been subjected to control. Secondly, the prescriber has been discouraged from using unnecessarily expensive brands of drugs, and thirdly, the consumer, the public, has been required to contribute to the cost of their prescriptions by paying a prescription charge. The reason for the concern about cost is the ever increasing size of the drug bill, shown in Figure 1 (see page 13).

1. The Pharmaceutical Industry

The manufacturers' prices and profits have been controlled since 1957 under rigorous price regulation schemes. The Department of Health requires all companies with sales of over £750,000 to submit an annual financial return which includes details of sales, costs and capital employed in the previous year. On this basis, the government can negotiate price reductions with the manufacturer. Prices and profits do have a considerable effect on the amount of money spent by the industry on sales promotion, a very important source of drug information. In July 1976, the government asked the pharmaceutical industry to reduce its sales

FIGURE 1

COST OF MEDICINES TO THE NATIONAL HEALTH SERVICE, 1950-1976



Source: NEDO Focus on Pharmaceuticals, London, HMSO, 1972 and ABPI Annual Reports

(These data are not corrected for inflation)

promotion to sales ratio from 14% in 1974 to 10% in 1979. This will reduce the amount of sales promotion and hence drug information provided by the pharmaceutical industry, and also may cause the collapse of some journals that rely heavily on drug advertising to reduce subscription costs or to circulate journals free of charge.

2. The Prescriber

Several government committees have investigated the possibility of discouraging wasteful and extravagant prescribing by doctors as a method of indirect price control. The first committee, the Joint Committee on Prescribing, was established in 1949.

Its terms of reference were to consider whether it was desirable and practicable to restrict or discourage prescribing of undesirable (or unethical) and unnecessarily expensive brands of standard drugs. The committee recommended that

> "there should be no absolute restriction on the prescribing by a general practitioner of any drug which in his opinion was necessary for the treatment of patients." 5

The committee also recommended that proprietary preparations should be classified in six categories. These were:

> "(1) New drugs of proved value not yet standard.
> (2) Proprietary brands of standard drugs, singly or in combination.
> (3) Standard preparations, and new remedies of proved value, in elegant form or vehicle.
> (4) Qualitative and/or quantitative modifications in the composition or combination of standard preparations, or new remedies of proved value, which are not accepted as therapeutically superior to preparations included either alone or in combination in the British Pharmacopoeia, the British Pharmaceutical Codex or the British National Formulary.

(5) Preparations not in the British Pharmacopoeia, British Pharmaceutical Codex or British National Formulary, which in the Committee's view have not been proved of therapeutic value.
(6) Preparations which are a combination of (4) and (5)." 6

By 1953, the Committee had classified all the then available drugs and had distributed the full classification to prescribers. The Standard Joint Committee on the Classification of Proprietary Preparations (the Cohen Committee) was established in 1954 to classify new products as they became available. After several years experience, the Cohen Committee became aware that there was a widespread and incorrect belief that these categories represented a decreasing order of therapeutic merit, category one drugs being the "best" and category six, the "worst".

Consequently the Cohen Committee revised the original classification as follows:

"Category N. New drugs of proved value which are not yet "standard". (The term "standard" is intended to mean preparations described in the British Pharmacopoeia, British Pharmaceutical Codex and British National Formulary.)

(This category replaces the old category 1.)

Category S. All preparations whose active therapeutic constituents are identical with or modifications of those of "standard" preparations.
Elegant preparations of drugs in category N.
Mixtures of drugs in category N with drugs in category S.

(This category replaces the old categories, 2,3 and 4.)

Category P. Preparations which are not "standard" for which prima facie evidence of therapeutic value is presented, but which the Committee cannot accept as of proved therapeutic value without further evidence, which must be provided within a period stipulated by the Committee.

(This is a new category.)

Category O. Preparations not "standard" which in the Committee's view have not been proved of therapeutic value.

(This category replaces the old category 5.)

Category H. Preparations which are a combination of drugs in category O with those in categories N, S, or P.

(This category replaces the old category 6.)" 6

The Committee recommended that preparations in categories N and P should be freely prescribable. Category S drugs could be prescribed if:

1. they were not foods or toilet preparations;
2. they were not advertised to the public directly;
3. the Department of Health and the manufacturer had agreed on their price.

The prescribing of drugs in categories O and H was actively discouraged by reminding doctors that if their prescribing was formally investigated, they might be required to justify the prescribing of these drugs. If the doctor's prescribing costs were considered excessive, remuneration could be withheld.

The Cohen Committee was wound up in 1964 because:

1. many doctors were confused about the classification system, particularly category S drugs;
2. some of the Committee's functions had been transferred to the newly established Committee on Safety of Drugs.

A new committee under the chairmanship of Professor MacGregor was set up to

> "advise on the classification of proprietary pharmaceutical preparations, with the object of helping doctors to decide which should be used in the treatment of their patients, and to identify those preparations, the prescribing of which appears to call for special justification." 7

The new committee immediately prepared its own system of

classification, since category P drugs were now assessed by the Committee on Safety of Drugs. The system of the MacGregor Committee was as follows

"Monograph preparations — Preparations whose active therapeutic constituents are identical with those of preparations described in the British Pharmacopoeia, British Pharmaceutical Codex or British National Formulary or which differ only slightly in physical form from such standard preparations, the difference being such as to have little or no therapeutic significance.

Category A. Sub-divided into:-

Category A.1. Preparations of single therapeutically active drugs which are acceptable formulations of substances (or active constituents of preparations) in the British Pharmacopoeia, British Pharmaceutical Codex or British National Formulary.
Category A.2. Preparations of single therapeutically active drugs which have been shown to the Committee's satisfaction to have an acceptable degree of efficacy in relation to their toxicity and therapeutic indications and which in the light of alternative available preparations can be recommended for use.
Category A.3. Acceptable preparations containing more than one drug where the main components are the active ingredients of monograph preparations and/or preparations in Category A.1. or A.2.

Category B. Sub-divided into:-

Category B.1. Preparations which, in the opinion of the Committee, on the evidence produced to it, have an unacceptable lesser degree of efficacy, or are of unacceptably greater toxicity, than alternative monograph preparations or preparations in Category A.
Category B.2. Unacceptable preparations which consist of or

> contain drugs which, in the view of the Committee, are not of proven efficacy." 7

Monograph and Category A preparations were recommended to be freely prescribable, but Category B drugs were actively discouraged by requiring doctors to justify prescriptions for these drugs if his prescribing was formally investigated, as before. The MacGregor Committee proposed to ensure that classification of new drugs would be made available to the prescriber as rapidly as possible, and that in the cases of impending appeal, publication would not be delayed as had been the case in the past.

The MacGregor classifications were published in the periodical Proplist, which was circulated to all doctors. Unfortunately, the semi-official publication, Prescribers' Journal, which contained articles on new and existing drugs assessed by an independent panel of clinicians and academics, failed to agree with the classification of a drug in Proplist on several occasions. (Prescribers' Journal is distributed free of charge to all doctors by the Department of Health & Social Security.) One example of this was Abicol (manufactured by Boots) which was placed in category B in Proplist, and in the same month was approved by Prescribers' Journal.[8] The confusion that was caused when the publications disagreed reduced the credibility of both publications.

The MacGregor Committee was eventually stood down in 1968, and the Medicines Commission has assumed its role of assessing product efficacy. Until recently, no part of the Medicines Commission had provided drug information to members of the medical profession (with the exception of the CSM's warnings

in connection with adverse reactions). The Committee on the Review of Medicines is the first to publish recommendations concerning any marketed product. At present there are no legal restrictions on what a doctor may prescribe for his patients.

In May 1976, a Private Members Bill calling for the restriction of the right of medical practitioners to prescribe certain hazardous drugs, gained its first reading.[9] The bill called for the Medicines Commission to draw up and maintain a list of hazardous or potentially hazardous drugs. The prescribing of listed products would be illegal, unless a doctor either attended four or more postgraduate sessions of three hours duration on clinical pharmacology, or kept proper records of his prescribing of listed products, making these available, on request, to a medical audit panel. This bill never became law, but it did propose that doctors should be required to learn about drugs in order to prescribe them.

The government has attempted in the past to influence the prescribing habits of doctors by providing them with information about marketed products. It appears unlikely that the Medicines Commission will resume this educative role or issue a restricted list of medicines available for prescribing, in the near future, for two reasons. Firstly, the medical profession are very anxious to retain their freedom of choice to prescribe any product. Secondly, the pharmaceutical industry insist that future innovation would be seriously inhibited, because any new medicine would be judged more harshly than one already on the market.[10]

The Department of Health has attempted to reduce the cost of drugs to the NHS by encouraging prescribers to use

the generic name of a drug on a prescription. This allows a pharmacist to choose which branded or unbranded product is dispensed, and the cost of the prescription is fixed by a wholesale list agreed by the Secretary of State and the chemist contractors. Prescribing by brand name removes this choice and fixes the cost of the prescription according to a price determined by the innovater, taking into account the cost of research and development. Although the Department of Health can reduce the price of a branded product if a manufacturers' profits are unacceptably high, it is generally accepted that approved-name products are cheaper than brand-name products. The pharmaceutical industry insist that prescribers use brand names on prescriptions, to ensure that the patient receives exactly the same formulation of any product. Slightly different formulations of the same active ingredients can have different biological availabilities in patients. Another reason for this insistance is that specification of the brand name protects the innovaters' research and development investment.

Drug information provided by the industry tends to use the brand name of a product, whereas information from other sources tends to use generic names.

In summary, the amount and content of drug information provided to the prescriber has been influenced by voluntary and legislative measures introduced by the government. The Medicines Act itself requires manufacturers to comply with certain standards in the provision of information. Concern about the cost and safety of pharmaceutical products has also indirectly improved the availability and provision of drug

information. In addition, to these measures, the ABPI require the members to follow a Code of Practice which controls sales promotion and provision of information. This will be discussed in Chapter 4, as this form of control is not enforced by the government.

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CHAPTER 2

USE OF DRUG INFORMATION SOURCES BY HOSPITAL DOCTORS

INTRODUCTION

There are numerous sources of information on drugs, but this does not necessarily mean that the information supplied by any particular source is adequate for the needs of the prescribing physician. To establish this, it is first necessary to discover which sources of information are used for prescribing and for learning about new drugs, and to look for deficiencies in the major existing sources.

The study of the use of drug information sources was carried out in a hospital environment. There were three reasons for this choice. Firstly, Sainsbury[1] and Eaton and Parish[2,3] have reported studies of the use of drug information sources by general practitioners. Both surveys indicated that general practitioners regard recommendations from consultants as a valuable source of information, and therefore, it is worthwhile discovering how the consultants obtain their information. Secondly, hospital doctors often require more specific and detailed drug information than their general practitioner colleagues. This occurs because diseases treated in hospital are often more serious than those treated in general practice. Finally, both information sources and prescribing habits are subjected to closer control in a hospital than in general practice

METHOD

1. The Sample

A questionnaire was distributed to 300 hospital doctors in

five Leicester area hospitals, during February, March and April of 1977. In addition, 50 hospital doctors were approached for parallel interviews. The sample was selected as shown in Table 1.

TABLE 1

SAMPLE OF HOSPITAL DOCTORS APPROACHED FOR INTERVIEW

Position	Total Number of doctors in the 5 hospitals	Doctors approached for interview No.	%
Consultant	128	18	14
Senior Registrar	21	3	14
Registrar	67	10	15
Senior House Officer	80	11	14
House Officer	19	3	16
Clinical Assistant	35	5	14
	350	50	14

2. The Questionnaire

The questionnaire consisted of 17 questions which fell into several well defined sections (see Appendix 2A).

The first three questions asked each doctor to state his medical qualifications, the medical school that he attended, the year that he graduated from medical school, his position in the hospital and the branch of medicine he practised.

This was followed by questions designed to discover which sources of drug information would be used to check on basic

prescribing details, and to find out about the existence and usefulness (or efficacy) of a new drug. The respondent was then asked about the value of resources that provide information on new drugs.

A series of questions were included to find out how many medical representatives were seen by each doctor and approximately how much direct mail was received each week. The respondent was also asked to assess the importance of these two sources of information, and to state whether he had ever used a pharmaceutical firm as an information source by writing for further information about a drug.

Finally each doctor was asked what information he would like to see readily available for each drug on the market. Several categories of information were suggested, and the respondents were asked to indicate which they considered important. They were also invited to make further suggestions.

The questionnaire took about ten minutes to complete. It was impossible to follow up non-responders to the questionnaire survey, because those returned were anonymous. A general reminder letter was sent to all 300 doctors, and this helped to improve the response rate.

3. The Interview

The interview used exactly the same questions that were included in the questionnaire. The advantage of the interview method over the distribution of questionnaires was that it enabled the respondents to discuss any points of particular interest to them. As interviews are expensive and time consuming, only a few could be carried out.

The interviews usually took about 15 minutes.

Non- responders were followed up with a reminder letter, and this was successful in improving the response rate to the interview survey.

RESULTS

1. Analysis of the Data

The completed questionnaire and interview forms were coded for analysis by computer, using FORTRAN IV.

The data obtained from the respondents were grouped according to their position in the hospital. This is usually rated to the qualifications held and experience in hospital medicine. House Officers (HO) are the least experienced hospital doctors and are normally undergoing an compulsory year of supervision, before their registration. Senior House Officers (SHO) have completed their pre-registration year and have decided to remain in the hospital rather than train for general practice. They usually study several specialities for short periods of time (e.g. six months in three specialities.) Registrars usually hold an appointment for three years in a particular speciality. Senior Registrars are normally appointed for about three years before being promoted to consultant status. Consultants have therefore usually studied in junior appointments for eight to ten years. They carry the most responsibility and are required to teach the junior doctors.

Clinical Assistants are general practitioners who work in the hospital for several hours each week.

For the purpose of this study, HOs, SHOs, registrars and clinical assistants were classified as junior doctors, and senior registrars and consultants were classified as senior

doctors.

2. Response

Fiftytwo percent of the questionnaires were completed and returned, and 48% of the doctors approached, agreed to be interviewed. Full details of the response rates are shown in Table 2 (see page 28). There was no significant difference between the two samples in the position held by the respondents.

3. Details of the Respondents' Medical Career

The medical qualifications held by the respondents were classified as follows:

1. basic qualifications - MB BS, MB ChB;
2 basic qualifications, plus a diploma in a particular specialism;
3. basic qualifications, plus membership of a Royal College, e.g. MRCP.

The number of doctors holding each type of qualification are shown in Table 3 (see page 29). As would be expected, junior doctors in both samples had lower qualifications than the senior doctors. However, there was no significant difference in the type of qualifications held by the interview and questionnaire respondents.

Each respondent stated where he received his medical training. This was either in:

1. the U.K.;
2. Western Europe, North America, Canada and Australasia;
3. rest of the world.

The results are shown in Table 4 (see page 30). More junior than senior doctors in both samples were trained outside the U.K. ($P<0.05$).

TABLE 2

RESPONSE TO THE QUESTIONNAIRE SURVEY

Position	Sample Size	Questionnaires Returned No.	%
Consultant	110	65	59
Senior Registrar	18	13	72
Registrar	57	27	47
SHO	69	27	39
HO	16	8	50
Clinical Assistant	30	15	50
Total	300	155	52

RESPONSE TO THE INTERVIEW SURVEY

Position	Sample Size	Doctors Interviewed No.	%
Consultant	18	8	50 *
Senior Registrar	3	1	50 *
Registrar	10	4	40
SHO	11	6	55
HO	3	-	-
Clinical Assistant	5	3	75 *
Total	50	22	48 *

* Two consultants, one senior registrar and one clinical assistant had left the Leicester area hospitals, and therefore the percentages shown were calculated assuming that the initial sample was 46 doctors.

TABLE 3

QUALIFICATIONS HELD BY HOSPITAL DOCTORS

Qualifications	Senior Doctors %	Junior Doctors %	Total Sample No.	%
Questionnaire Respondents				
Basic only	5	52	44	29
Basic plus diploma	4	13	13	8
Basic plus membership of a Royal College	91	35	98	63
Interview Respondents				
Basic only	11	62	9	41
Basic plus diploma	-	15	2	9
Basic plus membership of a Royal College	89	23	11	50

TABLE 4

PLACE OF TRAINING

Place of Training	Senior Doctors %	Junior Doctors %	Total Sample No.	%
Questionnaire Respondents				
U.K.	92	71	127	82
W. Europe, N. America, Canada, Australia, New Zealand	1	4	4	3
Rest of the World	5	25	23	14
not answered	1	-	1	1
Interview Respondents				
U.K.	89	46	14	64
W. Europe, N. America, Canada, Australia, New Zealand	11	8	2	9
Rest of World	-	46	6	27

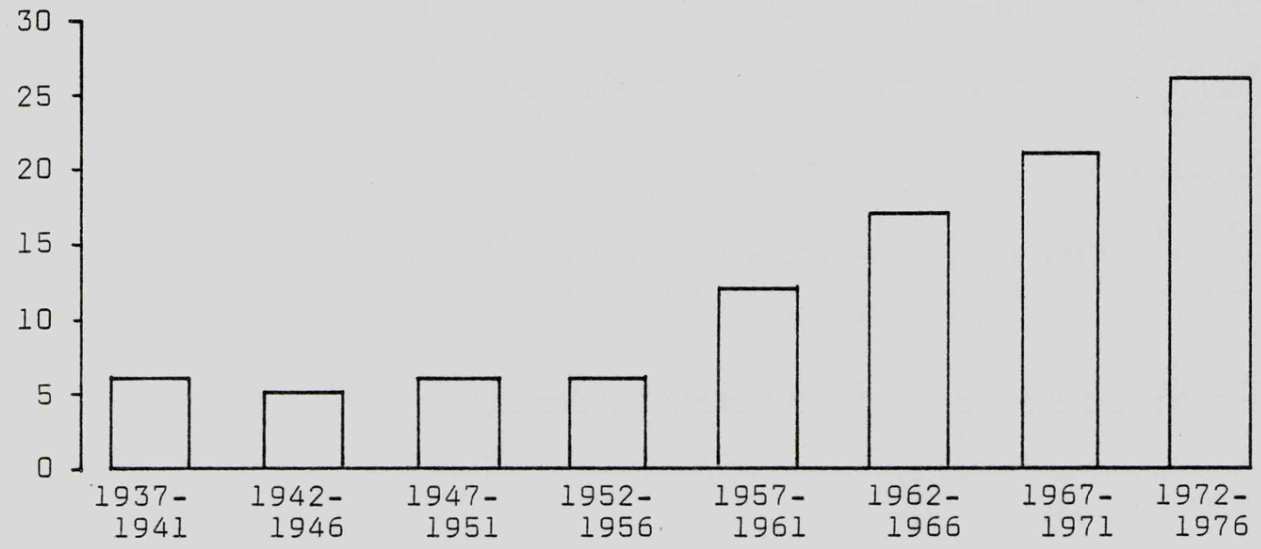
A higher proportion of doctors who were interviewed (than those replying to the questionnaire) were trained outside the U.K. ($P<0.05$).

Figure 1 shows the years that the respondents graduated from medical school (see page 31). No significant difference between the two samples were observed. Senior doctors by definition have been practising medicine for longer than junior doctors.

FIGURE 1

YEAR OF GRADUATION FROM MEDICAL SCHOOL

Questionnaire Respondents



Interview Respondents

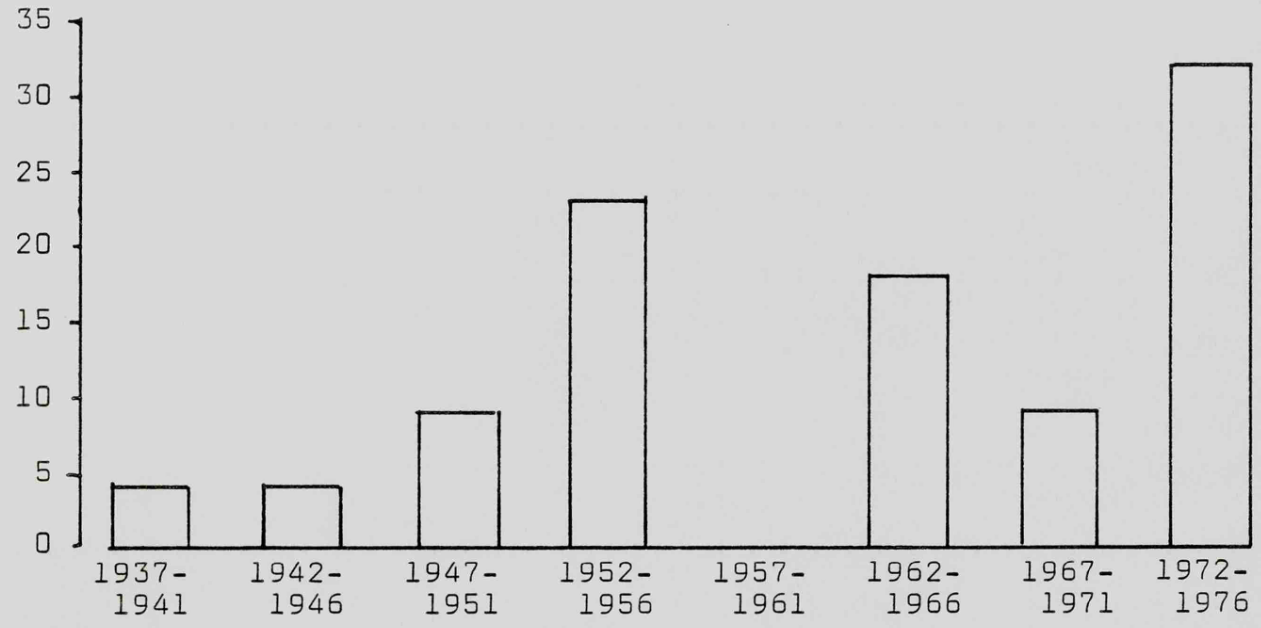


Table 5 shows the speciality that each of the respondents practised (see page 33). Since the number of doctors in each category was very small, and grouping the data would cause a loss of information, no statistical analyses of the data were carried out. Junior doctors usually train in several specialities before chosing a particular speciality for their career.

4. Sources of Information Used for Basic Prescribing Details

The hospital doctors were asked which sources of information they used to check on

1. indications (or uses of a drug)
2. dose
3. strength
4. contra-indications (or conditions for which the drug should not be used)
5. adverse effects
6. usefulness (or efficacy)
7. alternative drugs
8. drug interactions

Tables 6, 7 and 8 show the three sources that were quoted most often by the respondents (see pages 34, 35 and 36). The Monthly Index of Medical Specialities (MIMS) and the British National Formulary (BNF) are the sources used by the majority of doctors to check on dose, strength contra-indications, adverse effects and alternative drugs. MIMS was not used significantly more often than BNF, by either of the samples of respondents.

Senior hospital doctors tend to use the hospital pharmacy

TABLE 5

BRANCH OF MEDICINE PRACTISED

Speciality	Cons. No.	Sen. Reg. No.	Reg. No.	SHO No.	HO No.	Clin. Asst. No.	Total No.	Total %
Questionnaire Respondents								
Accident and Emergency	-	-	1	2	-	1	4	3
Anaesthetics	9	-	5	2	-	1	17	11
Cardiology	2	-	-	-	-	-	2	1
Chest Medicine	1	-	-	1	-	-	2	1
Dental/Oral Surgery	1	-	-	-	-	-	1	1
Dermatology	1	-	-	-	-	2	3	2
Ear, Nose and Throat	3	-	1	2	-	-	6	4
General Medicine	7	2	7	5	5	1	27	17
Geriatrics	3	-	-	1	-	-	4	3
Haematology	1	-	-	-	-	-	1	1
Mental Subnormality	2	-	-	-	-	1	3	2
Microbiology	1	-	1	-	-	1	3	2
Nephrology	-	-	1	-	-	-	1	1
Neurosurgery/Neurology	-	-	1	1	-	1	3	2
Obstetrics and Gynaecology	6	1	1	2	-	-	10	6
Ophthalmology	1	-	-	-	-	3	4	3
Orthopaedics	2	1	1	1	-	-	5	3
Paediatrics	3	1	1	4	-	-	9	6
Pathology	1	-	-	-	-	-	1	1
Plastic Surgery	2	-	1	-	-	-	3	2
Psychiatry	5	3	3	-	-	1	12	8
Radiology	1	2	1	-	-	-	4	3
Radiotherapy	1	-	-	-	-	-	1	1
Rheumatology	3	-	-	-	-	-	3	2
Surgery	6	3	2	4	2	-	17	11
Urology	1	-	-	1	-	-	2	1
Venerology	2	-	-	-	-	2	4	3
not answered	-	-	-	1	1	1	3	2
								100
Interview Respondents								
Accident and Emergency	-	-	-	2	-	-	2	9
Anaesthetics	1	-	1	-	-	1	3	14
Cardiology	1	-	-	-	-	-	1	5
Cytology	-	-	-	-	-	1	1	5
Dental/Oral Surgery	1	-	-	-	-	-	1	5
General Medicine	-	-	1	1	-	-	2	5
Geriatrics	1	-	1	-	-	-	2	9
Haematology	1	-	-	-	-	-	1	9
Mental Subnormality	-	-	1	-	-	-	1	5
Microbiology	1	-	-	-	-	-	1	5
Obstetrics and Gynaecology	-	-	-	1	-	-	1	5
Ophthalmology	-	-	-	1	-	-	1	5
Orthopaedics	1	-	-	-	-	-	1	5
Psychiatry	1	-	-	-	-	-	1	5
Radiotherapy	-	-	-	-	-	1	1	5
Surgery	-	1	-	1	-	-	2	9
								100

TABLE 6

SOURCES OF INFORMATION USED FOR BASIC PRESCRIBING DETAILS

Prescribing Information	Source	% of doctors using source * Questionnaire Respondents	Interview Respondents
Indications	BNF.....	31	27
	Textbooks.....	29	27
	MIMS.....	28	41
Dose	MIMS.....	62	64
	BNF.....	45	41
	ABPI Data Sheet Compendium.....	14	27
Strength	MIMS.....	54	55
	BNF.....	39	41
	ABPI Data Sheet Compendium.....	19	27
Contraindications	MIMS.....	48	55
	BNF.....	30	36
	ABPI Data Sheet Compendium.....	26	23
Adverse effects	MIMS.....	40	41
	BNF.....	27	41
	Textbooks.....	26	32
Usefulness	Textbooks.....	24	36
	BNF.....	22	23
	MIMS.....	19	
	Journal Articles.		32
Alternative drugs	MIMS.....	33	32
	BNF.....	28	
	Textbooks.....	25	23
	Journal Articles.		23
Drug interactions	Textbooks.....	27	18
	MIMS.....	26	36
	BNF.....	17	18
	Hospital Pharmacy Drug Interaction disc.....	17	18

* Totals of more than 100% in each category are due to respondents stating more than one source.

TABLE 7

DIFFERENCES IN THE SOURCES OF INFORMATION USED BY JUNIOR AND SENIOR DOCTORS FOR BASIC PRESCRIBING DETAILS

QUESTIONNAIRE RESPONDENTS

Prescribing Information	Source	% of doctors using source * Senior Doctors	Junior Doctors
Indications	MIMS	27	29
	BNF	24	38
	Textbooks	22	36
Dose	MIMS	59	65
	BNF	42	47
	Hospital Pharmacy	21	
	Textbooks		17
Strength	MIMS	51	56
	BNF	40	39
	ABPI Data Sheet Compendium	22	17
	Hospital Pharmacy	22	
Contraindications	MIMS	47	49
	ABPI Data Sheet Compendium	30	
	BNF	26	34
	Textbooks		27
Adverse effects	MIMS	40	40
	ABPI Data Sheet Compendium	28	
	BNF	24	29
	Textbooks		35
Usefulness	MIMS	21	17
	Journal Articles.	21	
	Textbooks	19	29
	BNF	19	25
Alternative drugs	MIMS	30	36
	BNF	24	33
	Textbooks	19	30
	Hospital Pharmacy	19	
Drug interactions	Hospital Pharmacy	27	
	MIMS	24	27
	BNF	19	16
	Textbooks		38

* Totals of more than 100% in each category are due to respondents stating more than one source.

TABLE 8

DIFFERENCES IN THE SOURCES OF INFORMATION USED BY JUNIOR AND SENIOR DOCTORS FOR BASIC PRESCRIBING DETAILS

INTERVIEW RESPONDENTS

Prescribing Information	Source	% of doctors using source * Senior Doctors	Junior Doctors
Indications	MIMS	56	31
	BNF	33	23
	Textbooks	22	31
Dose	MIMS	78	54
	BNF	55	31
	Hospital Pharmacy	44	
	ABPI Data Sheet Compendium		31
Strength	MIMS	78	39
	BNF	56	31
	Hospital Pharmacy	33	
	ABPI Data Sheet Compendium		31
Contraindications	MIMS	67	45
	BNF	44	31
	Hospital Pharmacy	22	
	ABPI Data Sheet Compendium		31
Adverse effects	MIMS	67	
	BNF	44	39
	Textbooks	22	39
	ABPI Data Sheet Compendium	22	31
Usefulness	Textbooks	33	39
	MIMS	33	
	Journal Articles.	33	39
	BNF		23
Alternative drugs	MIMS	44	23
	Recommendations from Colleagues.	33	
	Journal Articles.	22	23
	Textbooks	22	23
Drug interactions	MIMS	44	31
	BNF	33	15
	Hospital Pharmacy	33	
	Drug Interaction disc		31

* Totals of more than 100% in each category are due to respondents stating more than one source.

as an information source after MIMS and BNF, whereas junior doctors rely more often on textbooks.

5. Sources of Information Used to Learn about New Drugs

This question was designed to find out which sources of information were used to learn about the existence and usefulness (or efficacy) of a new drug. A list of possible sources was provided. This included subscription and controlled circulation publications, information originating from drug firms and advice from professional colleagues.

Tables 9, 10 and 11 show the proportion of doctors using particular sources (see pages 38, 39 and 40). It was decided to list only the sources used by at least 40% of the respondents. Senior doctors who responded to the questionnaire were found to rely heavily on specialist journals whereas junior doctors tended to use MIMS to learn about the existence of a drug and the British Medical Journal to learn about its efficacy ($P<0.001$). All clinical assistants used MIMS to find out about existence, and both BNF and the Prescribers' Journal for information about efficacy.

The use of general medical journals by senior and junior doctors who responded to the questionnaire is also significantly different ($P<0.001$). Senior doctors were found to use The Lancet whereas junior doctors tended to use the Drug and Therapeutics Bulletin and the Adverse Drug Reaction Bulletin.

The senior doctors who were interviewed relied on specialist journals to learn about new drugs ($P<0.05$). Junior doctors tended to use firm meetings to learn about the existence of a drug and the British Medical Journal and the Prescribers'Journal to learn about product efficacy. There was no difference in the

TABLE 9

SOURCES OF INFORMATION USED TO LEARN ABOUT NEW DRUGS

Source	% of doctors using source to learn about the existence of a drug	usefulness of a drug	existence of a drug	usefulness of a drug
	Questionnaire Respondents		Interview Respondents	
MIMS	85	52	50	..
British Medical Journal	73	77	50	55
Journal Articles	68	88	95	91
Recommendations from Colleagues	66	69	..	..
BNF	57	57	45	..
Representatives	55	42	..	..
ABPI Data Sheet Compendium	55	41	50	..
Drug firm mail	51	..	..	..
Prescribers' Journal	49	69	59	..
British Journal of Hospital Medicine	48	59	41	..
Hospital Pharmacy	44	46	..	..
Post Graduate meetings	43	46	..	..
Advertisements in medical journals	..	..	41	..

Only sources used by at least 40% of the respondents are included in the Table.

TABLE 10

SOURCES OF INFORMATION USED BY QUESTIONNAIRE RESPONDENTS TO LEARN ABOUT NEW DRUGS

Source	% of doctors using source to learn about the existence of a drug	usefulness of a drug	existence of a drug	usefulness of a drug
	Senior Doctors		Junior Doctors	
Specialist Journals	108 *	132 *	..	44
MIMS	76	53	94	51
British Medical Journal	74	78	71	75
Recommendations from Colleagues	64	68	68	70
ABPI Data Sheet Compendium	56	47	53	..
Representatives	54	..	56	47
British Journal of Hospital Medicine	54	65	42	52
Prescribers' Journal	53	73	46	65
BNF	53	50	62	65
Lancet	51	55	..	..
Hospital Pharmacy	46	56	42	..
Drug firm mail	45	..	57	..
Post Graduate meetings	..	45	47	48
Drug and Therapeutics Bulletin	..	..	46	51
Advertisements in medical journals	..	..	44	..
Adverse Drug Reaction Bulletin	..	..	..	48

Only sources used by at least 40% of the respondents are included in the Table.

* Totals of more than 100% are due to respondents mentioning more than one specialist journal.

TABLE 11

SOURCES OF INFORMATION USED BY INTERVIEW RESPONDENTS TO LEARN ABOUT NEW DRUGS

Source	% of doctors using source to learn about the existence of a drug	usefulness of a drug	existence of a drug	usefulness of a drug
	Senior Doctors		Junior Doctors	
Specialist Journals	178 *	178 *	..	..
Prescribers' Journal	89	44	..	62
British Medical Journal	67	67	..	46
British Journal of Hospital Medicine	67	..	..	..
MIMS	67	..	..	..
BNF	56	..	..	..
ABPI Data Sheet Compendium	56	..	46	..
Recommendations from Colleagues	56	44	..	..
Lancet	56	44	..	..
Post Graduate meetings	44	..	..	..
Advertisements in medical journals	..	..	46	..
Drug firm mail	..	..	46	..
Drug firm meetings	..	..	46	..

Only sources used by at least 40% of the respondents are included in the Table.

* Totals of more than 100% are due to respondents mentioning more than one specialist journal.

use of general medical journals by senior and junior interview respondents.

Both samples of respondents tended to use sources of information provided by the pharmaceutical industry to learn about the existence of a new drug, although this was followed closely by medical journals. Professional journals alone were considered useful to learn about the efficacy of a new drug.

6. Opinions of Information concerning Newly Introduced Drugs

Doctors in both samples were asked whether they felt able to obtain an unbiased assessment of a newly introduced drug. The results are shown in Table 12.

TABLE 12

OPINIONS OF BIAS IN INFORMATION ABOUT NEW DRUGS

Ability to Obtain an Unbiased Assessment	Senior Doctors %	Junior Doctors %	Total Sample No.	Total Sample %
Questionnaire Respondents				
Able to obtain an unbiased assessment	56	45	79	51
Unable to obtain an unbiased assessment	37	48	66	43
Cannot answer	3	3	4	3
Not answered	4	4	6	3
Interview Respondents				
Able to obtain an unbiased assessment	11	23	4	18
Unable to obtain an unbiased assessment	67	62	14	64
Cannot answer	22	15	4	18

An interesting significant difference appeared between the questionnaire and interview responses ($P<0.02$). Of the questionnaire respondents, 51% stated that they could obtain an unbiased assessment, but only 18% of the doctors interviewed felt able to do so.

Those doctors who did feel able to obtain an unbiased assessment were asked to state which sources they would use. The results are shown in Table 13.

TABLE 13

SOURCES USED TO OBTAIN AN UNBIASED ASSESSMENT OF NEW DRUGS

Sources	Senior Doctors %*	Junior Doctors %*	Total Sample No.	%*
Questionnaire Respondents				
Journals	93	97	75	95
Medical colleagues	39	31	28	35
Pharmacists	9	-	4	5
Drug firms	9	11	8	10
Others	7	-	3	4
not answered	5	-	2	3
Interview Respondents				
Journals	100	100	4	100
Medical colleagues	100	-	1	25
Drug firms	-	33	1	25

* Expressed as a percentage of those doctors who felt able to obtain an unbiased assessment of a new drug.

No differences in the sources used by either junior and senior doctors, or the interview and questionnaire respondents were observed. The majority of respondents used medical journals to obtain an unbiased assessment.

The respondents who felt unable to obtain an unbiased assessment of a new drug were asked to state why they could not do so. The results are shown in Table 14.

TABLE 14

REASONS FOR BEING UNABLE TO OBTAIN AN UNBIASED ASSESSMENT OF A NEWLY INTRODUCED DRUG

Reasons	Senior Doctors %*	Junior Doctors %*	Total Sample No.	%*
Questionnaire Respondents				
Sponsorship of trials by drug firms cause bias	45	27	23	34
Initial assessment of a new drug is usually too over enthusiastic	28	19	15	23
Too little objective information is available	14	27	14	21
Assessment is too time consuming	-	8	3	5
not answered	19	16	11	16
Interview Respondents				
Sponsorship of trials by drug firms cause bias	33	62	7	50
Initial assessment of a new drug is usually too over enthusiastic	50	25	5	36
Too little objective information is available	17	13	2	14

* Expressed as a percentage of those doctors who felt unable to obtain an unbiased assessment of a new drug.

Again there was no difference in the reasons given (for being unable to obtain an unbiased assessment) by either senior and junior doctors or questionnaire and interview respondents. The main reason for this was the belief that sponsorship of clinical trials by manufacturers would tend to cause the trialists to become biased in their assessment of a new drug.

7. The Value of Published Reports of Clinical Trials

The respondents were asked whether they considered that published reports of clinical trials were a useful source of information on new drugs. If the answer was no, the respondent was asked why he held this view. New drugs were considered to be either newly introduced drugs or drugs that were new to the doctor. The results of these two questions are shown in Table 15 and 16 (see pages 45 and 46).

Significantly more of the questionnaire than interview respondents considered that reports of clinical trials were a useful source of information about new drugs ($P<0.02$). Junior doctors who responded to the questionnaire were less likely to consider reports useful than senior doctors ($P<0.01$). However, there was no significant difference in the opinion of the usefulness of trial reports between senior and junior doctors, in the sample interviewed. The main reason for considering that the reports were not useful, was the complaint that the reports were too long and were irrelevant to clinical practice.

8. Medical Representatives as a Source of Information about Drugs

Medical representatives were considered a useful source of information by 55% of the questionnaire respondents and by 35%

TABLE 15

OPINIONS OF THE USEFULNESS OF PUBLISHED REPORTS OF CLINICAL TRIALS

Opinions of the Reports	Senior Doctors %	Junior Doctors %	Total Sample No.	%
Questionnaire Respondents				
Useful	81	73	119	77
Not useful	6	19	20	13
Cannot answer	12	5	13	8
not answered	1	3	3	2
Interview Respondents				
Useful	56	54	12	55
Not useful	22	38	7	32
Cannot answer	22	8	3	13

TABLE 16

REASON FOR NOT CONSIDERING PUBLISHED REPORTS OF CLINICAL TRIALS A USEFUL SOURCE OF INFORMATION ABOUT NEW DRUGS

Reason	Senior Doctors %*	Junior Doctors %*	Total Sample No.	%*
Questionnaire Respondents				
Reports too long and not relevant to clinical practice	60	60	12	60
Too little time available to read reports	20	33	6	30
Sponsorship of trials by drug firms causes bias	20	7	2	10
Interview Respondents				
Reports too long and not relevant to clinical practice	50	40	3	43
Too little time available to read reports	-	40	2	29
Sponsorship of trials by drug firms causes bias	50	20	2	29

* Expressed as a percentage of those doctors who did not consider reports of clinical trials a useful source of information.

of those who were interviewed, for learning about the existence of a new drug. Both samples considered them less important for learning about the efficacy of a product.

Several questions were asked to assess the contact that medical representatives had with hospital doctors. Tables 17, 18 and 19 show the number of representatives that approach the respondents and the number that are granted an interview (see pages 48, 49 and 50).

Clinical assistants were approached by more representatives for a personal interview than all other hospital doctors, in both the questionnaire and interview samples ($P<0.001$). However, clinical assistants did not see significantly more representatives than the other hospital doctors.

Junior doctors who responded to the questionnaire tended to be approached, and to see, medical representatives with other doctors present, whereas senior doctors tended to see them alone ($P<0.02$). Table 19 shows that the majority of doctors were approached by 1-3 representatives, and saw most, or all, of them.

There was an important dichotomy in attitudes to representatives as shown in Table 20 (see page 51).

Many doctors do not think that they would lose an important source of information if they did not see any representatives, but those doctors who saw most, or all, of the representatives that approached them, asserted that they form a useful source of information ($P<0.001$).

It was interesting to note that the questionnaire respondents who held some medical qualification in addition to the basic medical degree tended not to consider representatives a useful source of information ($P<0.05$). Questionnaire respondents who

TABLE 17

THE NUMBER OF REPRESENTATIVES THAT APPROACH HOSPITAL DOCTORS FOR AN INTERVIEW EACH MONTH

Number of Representatives	Senior Doctors %	Junior Doctors %	Total Sample No.	Total Sample %	(Clin. Assist. %)
Questionnaire Respondents					
a. Personally					
none	13	13	20	13	7
1-3	55	45	78	50	7
4-6	19	14	26	17	33
more than 6	8	8	12	8	33
not answered	5	19	19	12	20
b. With Other Doctors Present					
none	19	14	26	17	20
1-3	9	44	41	26	7
4-6	3	10	10	7	7
more than 6	-	3	2	1	7
not answered	69	29	76	49	60
Interview Respondents					
a. Personally					
none	11	15	3	14	-
1-3	56	23	8	36	33
4-6	-	8	1	4	-
more than 6	22	15	4	18	67
do not know	11	38	6	27	-
b. With Other Doctors Present					
none	22	31	6	27	67
1-3	11	46	7	32	-
do not know	67	23	9	41	33

* Although clinical assistants are included in the data shown for junior doctors, the number of representatives that approach them is shown in a separate column, because they tended to be approached by more than other hospital doctors.

TABLE 18

THE NUMBER OF REPRESENTATIVES SEEN BY HOSPITAL DOCTORS EACH MONTH

Number of Representatives seen	Senior Doctors %	Junior Doctors %	Total Sample No.	%
Questionnaire Respondents				
a. Personally				
none	21	10	24	15
some	33	35	53	34
most	33	31	50	32
all	13	4	13	8
not answered	-	19	15	10
b. With Other Doctors Present				
none	13	10	18	12
some	9	34	33	21
most	5	22	21	14
all	1	3	3	2
not answered	73	31	80	52
Interview Respondents				
a. Personally				
none	11	31	5	23
some	56	31	9	41
most	22	-	2	9
all	11	8	2	9
not approached by any	-	31	4	18
b. With Other Doctors Present				
none	11	31	5	23
some	11	23	4	18
most	11	8	2	9
all	-	23	3	14
not approached by any	67	15	8	36

TABLE 19

COMPARISON OF THE NUMBER OF REPRESENTATIVES THAT APPROACH HOSPITAL DOCTORS FOR AN INTERVIEW EACH MONTH, AND THE NUMBER THAT ARE SEEN

No. Representatives approaching doctors / No. seen	None %	1-3 %	4-6 %	more than 6 %	not answered %
Questionnaire Respondents					
a. Personally					
none	9	3	1	1	2
some	-	20	8	3	4
most	-	22	6	3	1
all	-	6	1	1	-
not answered	4	-	-	-	6
b. With Other Doctors Present					
none	9	1	-	-	-
some	-	14	3	1	3
most	-	10	3	-	1
all	-	1	-	-	-
not answered	8	-	-	-	44
Interview Respondents					
a. Personally					
none	14	5	-	5	-
some	-	14	5	14	9
most	-	9	-	-	-
all	-	9	-	-	-
not approached by any	-	-	-	-	18
b. With Other Doctors Present					
none	14	-	-	-	9
some	-	9	-	-	5
most	-	9	-	-	-
all	-	14	-	-	-
not approached by any	14	-	-	-	27

TABLE 20

OPINIONS OF MEDICAL REPRESENTATIVES

Opinion	Senior Doctors %	Junior Doctors %	Total Sample No.	Total Sample %
Questionnaire Respondents				
Representatives are important	41	53	73	47
Representatives are not important	56	43	77	50
Cannot answer	1	-	1	1
not answered	1	4	4	3
Interview Respondents				
Representatives are important	44	23	7	32
Representatives are not important	56	62	13	59
Cannot answer	-	15	2	8

qualified in Britain tended to attach less importance to representatives than doctors qualifying elsewhere ($P<0.01$).

9. Direct Mail as a Source of Information about Drugs

Hospital doctors were asked how much direct mail from drug companies they received in the post, in an average week, both at home and at the hospital. Table 21 shows the results (see page 53).

Clinical assistants who responded to the questionnaire receive significantly more direct mail at their home than all other hospital doctors ($P<0.05$). Senior doctors tend to receive more mail at the hospital than junior doctors ($P<0.05$). Eighty two percent of the questionnaire respondents and 92% of the sample interviewed received direct mail both at home and at the hospital. The majority of doctors received 1-5 items per week in both places.

Doctors were asked whether they ever kept direct mail advertisements and data sheets. Although data sheets are not advertisements, they can be sent through the post, and hence they were included in the same section of the questionnaire as direct mail. (A data sheet is a legal document; its format and information content is discussed in Chapter 1.) The results are shown in Table 22 (see page 54).

The majority of doctors do not keep direct mail advertisements whereas the majority do keep data sheets. Doctors who were interviewed were significantly more likely to keep data sheets than questionnaire respondents ($P<0.02$). One percent of the questionnaire respondents and 9% of those interviewed claimed that they did not receive data sheets, despite the legal requirement for pharmaceutical firms to provide every prescribing

TABLE 21

QUANTITY OF DIRECT MAIL RECEIVED EACH WEEK BY HOSPITAL DOCTORS

Number of Items	Senior Doctors %	Junior Doctors %	Total Sample No.	Total Sample %	(Clin. Assist. %)
Questionnaire Respondents					
a. at home					
none	9	9	14	9	13
1-5	67	53	93	60	7
6-10	12	5	13	8	13
more than 10	-	13	11	7	60
not answered	12	19	24	15	7
b. at the hospital					
none	4	12	13	8	27
1-5	68	64	102	66	33
6-10	14	4	14	9	13
more than 10	3	-	2	1	-
not answered	10	21	24	15	27
Interview Respondents					
a. at home					
none	-	8	1	4	-
1-5	56	46	11	50	33
6-10	11	15	3	14	33
more than 10	11	8	2	9	33
do not know	22	23	5	23	-
b. at the hospital					
none	11	8	2	9	-
1-5	22	54	9	41	33
6-10	11	-	1	4	-
do not know	56	38	10	45	67

* Although clinical assistants are included in the data shown for junior doctors, the quantity of direct mail that they receive is shown in a separate column, because they tended to receive more than other hospital doctors.

TABLE 22

DECISION TO KEEP DIRECT MAIL ADVERTISEMENTS AND DATA SHEETS

Decision	Senior Doctors %	Junior Doctors %	Total Sample No.	Total Sample %
Questionnaire Respondents				
a. Direct Mail				
keep direct mail	36	29	50	32
do not keep direct mail	63	69	102	66
do not receive any	-	-	-	-
not answered	1	3	3	2
b. Data Sheets				
keep data sheets	72	66	107	69
do not keep data sheets	28	30	45	29
do not receive any	-	1	1	1
not answered	-	3	2	1
Interview Respondents				
a. Direct Mail				
keep direct mail	11	38	6	27
do not keep direct mail	89	54	15	68
do not receive any	-	8	1	4
b. Data Sheets				
keep data sheets	89	85	19	86
do not keep data sheets	11	-	1	4
do not receive any	-	15	2	9

doctor with a data sheet before promoting a new product.

Almost half of the respondents in both samples felt that they would lose an important source of information if they did not receive any direct mail (see Table 23, page 56). Clinical assistants responding to the questionnaire more often considered that direct mail was an important source than other hospital doctors ($P<0.01$). As would be expected, those respondents who kept direct mail were more likely to consider that it was an important source ($P<0.001$).

Questionnaire respondents who considered medical representatives a useful source of information also tended to consider that direct mail was a useful source ($P<0.01$).

Doctors who qualified in Britain were less likely to consider that direct mail was an important source of information than doctors qualifying elsewhere ($P<0.05$). Also, questionnaire respondents who qualified before 1956 tended to consider that direct mail was important ($P<0.02$).

10. Direct Contact with a Pharmaceutical Firm

It was noted that, although 65% of the questionnaire respondents had, at some stage in their medical career, written to a pharmaceutical firm for further information about a drug only eight percent did so on a regular basis. Ninetytwo percent of the doctors had written for information to answer a specific problem. Sixtyfour percent of the doctors who were interviewed had written to a pharmaceutical firm for further information and 21% did so on a regular basis. Eightytwo percent had written for specific information. As would be expected, senior doctors in both samples were more likely to have contacted a firm in this way ($P<0.01$). Clinical assistants in both samples had

TABLE 23

OPINIONS OF DIRECT MAIL

Opinion	Senior Doctors %	Junior Doctors %	Total Sample No.	Total Sample %
Questionnaire Respondents				
Direct mail is important	45	48	72	47
Direct mail is not important	54	49	80	52
not answered	1	3	3	2
Interview Respondents				
Direct mail is important	22	46	8	36
Direct mail is not important	67	46	12	54
Cannot answer	11	7	1	4
Do not receive any	-	1	1	4

contacted drug firms to a greater extent than other junior doctors ($P<0.05$).

11. Use of References cited on Drug Advertisements

References are often quoted on drug advertisements and therefore the reader can substantiate the claims of the referenced information. Thirtynine percent of the questionnaire respondents and 23% of the doctors who were interviewed had followed up an advertisement at least once in their medical career. Senior doctors in both samples were more likely to have checked a reference than junior doctors ($P<0.05$).

There appears to be a just reward for the effort of following up a reference, because 77% of the questionnaire respondents and 80% of the doctors interviewed considered the information that they obtained was useful.

12. Information of Basic Importance and Prescribing

Each doctor was asked about the information that he would like to see readily available for each drug on the market. A prompt list which included 14 items was provided. At least 79% of respondents in both samples considered that the items shown in Table 24 were important (see page 58). Several additional items of information were suggested by 31% of the questionnaire respondents and 59% of the doctors interviewed, and these are shown in Table 25 (see page 59).

DISCUSSION

1. Problems of Questionnaire and Interview Design

It is very difficult to obtain exact data about the use of

TABLE 24

INFORMATION REQUIRED FOR EACH MARKETED DRUG

Items of Information Required	Questionnaire Respondents No.	%	Interview Respondents No.	%
Approved name	149	96	21	95
Indications	144	93	20	91
Dose	150	97	22	100
Strength	139	90	21	95
Route and time of administration	143	92	22	100
Contraindications	150	97	21	95
Special precautions	145	94	21	95
Any reported adverse reactions	140	90	21	95
Usefulness (or efficacy)	122	79	20	91
Overdosage treatment	129	83	20	91
Drug interactions	148	95	21	95
Presentation (e.g. tablet etc.)	122	79	22	100
Cost	134	87	20	91
Absorption and distribution of the drug in the blood and body tissues and excretion of the drug	130	84	20	91

TABLE 25

SUGGESTED ADDITIONAL ITEMS OF INFORMATION REQUIRED FOR EACH MARKETED DRUG

Additional Items	Questionnaire Respondents %	Interview Respondents %
Objective comparision with other drugs	11	18
Details of mode of action	7	14
Pharmacological precautions	5	18
Dosage level in paediatric and geriatric patients	5	9
All known brand names	5	4
Pharmaceutical precautions	3	4
Concise list of references to the literature	3	4
Tablet identification	3	-
Chemical data	3	4
Objective discussion of clinical trial reports	1	-
Reasons for the introduction of the drug on to the market	1	-
Length of time the drug has been in use	1	-
Bioavailability	-	4
Legal category	-	4
Package quantities	-	4
Range of sensitive organisms (antibiotics)	-	4

various sources of information as rigid patterns of information gathering are often upset by the availability of the information, its particular relevance at the time of searching, and the appearance of information by chance (therefore unplanned). In addition, there may well be some slight stigma attached to the use of drug information sources produced by the pharmaceutical industry, particularly promotional material. In an attempt to avoid this, the questionnaires were distributed without any identification mark and the replies were returned anonymously. It was recognised, however, that there must be certain limitations placed on the data collected, as they probably cover a range from actual to ideal behaviour. Respondents may have provided answers which would make them appear more intelligent.

A factor that may have influenced the response rate was the difficulty in ensuring that the original sample of doctors had received their copy of the questionnaire or the letter asking them for an interview. As some doctors hold short-term appointments in the hospital, the lists of doctors available are not always up-to-date and complete. It is possible that some of the doctors who had taken up posts just before the survey commenced were not included. Similarly, doctors who did not receive either a questionnaire or a request for an interview, because they had left the hospitals were classified as non-respondents. In an attempt to determine the number of these non-respondents, the secretaries in each hospital department were asked whether the lists used were accurate. Unfortunately, the majority of the secretaries were unable to provide this information. For this reason, the response rate might have been higher than it appeared to be.

2. Other Studies

Bauer and Wortzel noted in 1966 that

> "asking doctors where they learn about drugs has been popular activity over the last decade and a half (i.e. 1950-1965)." 4

Almost as many studies again have been carried out since 1965, totalling 24 since 1950. Appendix 2B lists the investigators and the type of study that they carried out. Several authors[4-8] have reviewed the numerous investigations. All of these studies have concentrated on the use of drug information by general practitioners. Only five of the 24 studies were conducted in Britain, (the remaining 19 were carried out in the U.S.). Since the sources of drug information available to doctors in the U.S. differ from those available in the U.K., no comparison of the results obtained by the British and American studies were made.

The majority of these 24 studies attempted to discover exactly how the respondent adopted a new drug. Not only did this approach assume that drug adoption occurred as a result of a logical series of events, rather than a combination of deliberate and chance gathering of information, but that the respondents had perfect recall of the events leading up to adoption.

Although some of the data obtained from the five British studies were compared with the results of this study, it was noted that the information requirements of hospital doctors and general practitioners were often different. Table 26 shows several factors which would affect the type of drug information that would be required by each group of doctor. Seltzer and Riley[9] found that there was a difference in approach to the use of antibiotics by hospital doctors and general practitioners. Hospital doctors rated the sensitivity of the causitive organism

to the antibiotic as the most important factor whereas general practitioners considered clinical effectiveness of the product as the most important criterion.

TABLE 26

FACTORS AFFECTING THE INFORMATION REQUIREMENTS OF HOSPITAL DOCTORS AND GENERAL PRACTITIONERS

Category	Similarities	Dissimilarities
Type of patient	Sex & age group	G.P. - patient often consulting with complaint for the first time. Serious cases usually referred to hospital doctors. Hospital Doctor (HD) - patient often previously treated. Tend to treat serious cases.
Diagnosis capability		G.P. - limited facilities H.D. - extensive facilities available
Status factors		G.P. - rewards for increased knowledge usually financial and small. H.D. - positive incentive to increase knowledge for career progression. Consultant - role as a teacher
Type of medicine practised		G.P. - general medicine (specialisation in group practice is rare). H.D. - specialised or aiming towards specialisation.

The clinical assistant provides a link between the general practitioner and the hospital doctor, and hence the sources of information that he uses are of interest.

3. Sources of Information Used for Basic Prescribing Details

Hospital doctors tend to rely on sources of information that are provided free of charge, either sponsored by the pharmaceutical industry (MIMS), or circulated by the Department of Health and Social Security (BNF), when checking basic prescribing details. MIMS is used more often to check on dose, strength, contra-indications, adverse effects, alternative drugs and drug interactions, whilst BNF is used more frequently to check on indications and efficacy. Both of these sources are pocket-sized reference books, but MIMS has two advantages over BNF:

a. MIMS is more up-to-date, being printed monthly, whereas BNF is published every two to three years;

b. MIMS contains a therapeutic index, permitting an easy transition from diagnosis to drug therapy.

It was noted that MIMS was used to check on adverse effects, which it does not, in fact, routinely list. (BNF contains a section on adverse reactions to drugs and hazards of drugs in pregnancy, lactation and the newborn, but the amount of information is limited.) It seems therefore that doctors tend to use MIMS as a therapeutic text, rather than a guide to dosage, which is its basic function. This may be partly due to inertia, but also stems from less easy access to other sources of information.

Eaton and Parish[2] found that BNF and MIMS would be used by the majority of general practitioners to select an appropriate drug for treatment and to check on dosage or strength of a drug. These sources would also be used to check on contra-indications and adverse effects. Unfortunately, this

latter result is confusing because both BNF and MIMS do list contraindications but as stated above, only BNF provides information on adverse effects.

It appears that both hospital doctors and general practitioners use MIMS and BNF to check basic data, once a drug has been accepted into the prescribing repertoire.

4. Sources of Information Used to Learn about New Drugs

The decision to prescribe a drug can be considered to take place in two stages. Firstly, the doctor must become aware of the new drug's existence. Secondly, he must gather and evaluate information on the efficacy of the product before using it.

Hospital doctors tend to use sources provided by the pharmaceutical industry to learn about the existence of a new drug. This is partly because there is a lack of information about new drugs from other sources, and partly because new drugs are usually launched with massive promotional campaigns aimed at producing awareness. To learn about the efficacy of a product, sources provided by the medical profession are used. These include both articles in medical journals and oral recommendations.

A similar result was obtained in the surveys of information sources used by general practitioners carried out by Sainsbury[1] and Eaton and Parish[2]. One interesting difference is the greater reliance of general practitioners on medical representatives to learn about the existence of new drugs.

The more highly qualified hospital doctors also tended to be more specialised and hence they tended to use specialist journals to a greater extent than junior doctors for finding out

about product efficacy.

Doctors who believed that representatives and direct mail were an important source of information, also tended to use these sources to learn about the existence of a drug. Although this result was not surprising, it did suggest that the respondents were consistent in their answers to the questionnaire or the interview.

5. Opinions of Information Concerning Newly Introduced Drugs

Despite the majority of information about new drugs being promotional, about half of the questionnaire respondents felt that they could obtain an unbiased assessment of a new drug. The reason for this dichotomy is unclear.

A much greater proportion of doctors who were interviewed felt unable to obtain an unbiased assessment. It is possible that the interview situation caused this difference, but as a greater proportion of the sample of doctors interviewed did not consider that either direct mail or representatives were an important source of information, the majority of this sample appeared to have a greater distrust of commercially produced information.

Eaton and Parish[3] also found that general practitioners were divided in their opinions about being able to obtain unbiased assessments of new drugs.

6. Opinions of Medical Representatives

Sainsbury found that 70% of the general practitioners who responded to the government survey felt that representatives were an important source of information. Eaton and Parish[2]

confirmed this result, as 67% of their respondents also held this view. The relatively smaller percentages of hospital doctors that considered representatives important, may indicate that they are considerably less influential in the hospital environment.

It was interesting to note that there was a tendency for lower qualified doctors and those who qualified outside the U.K. to consider that representatives were important. This perhaps suggests that these doctors had different attitudes to the pharmaceutical industry.

7. Opinions of Direct Mail

Opinions as to whether direct mail was an important source of information were equally divided between those who thought that it was, and those who thought that it was not. Clinical assistants were more likely to consider that direct mail was an important source than other hospitals doctors. This was probably because they tended to receive more than other groups of hospital doctors.

Again, doctors qualifying outside the U.K. were more likely to consider mail important, possibly because they had different attitudes to pharmaceutical promotion.

8. Opinions of Referenced Material on Drug Advertisements

Stimson[10] has expressed concern about the availability of the references cited in drug advertisements. This may be one reason why the majority of doctors do not follow up the references cited. Since references often lead to reports of clinical trials, (Stimson[10] found that 63% of a sample did so) they could be considered a useful starting point in the process

of evaluation of drugs.

9. Information Requirements of Hospital Doctors

Although many drug information sources aim to meet the needs of the prescribing physician, this survey suggests that no single source currently available is entirely adequate. It appears that an easily accessible (preferably free) pocket-sized drug reference manual is required. It should contain at least those items mentioned in Table 24, and be updated at regular intervals. The material should be presented in such a manner as to emphasise a high degree of impartiality of the contents.

Such a volume could not readily provide answers to more detailed queries concerning drug therapy. Recent studies suggest that existing drug information services run by clinical pharmacologists and pharmacists possess considerable potential as providers of detailed information on drugs.[11,12] This study suggests that this potential is not yet being fully exploited. Another advantage of the drug information service is its ability to meet the information needs of para-medical workers. Couper and Roxburgh[13] reported that nurses do require a certain amount of drug information, particularly details of storage conditions and shelf life.

A revised drug information manual, supported by a high quality information service could form the basis for an efficient back-up service for the prescribing physician.

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APPENDIX 2A

QUESTIONNAIRE

The Use of Drug Information

Sources by Hospital Doctors

This questionnaire is part of a larger project investigating the quality and availability of the various sources of drug information with a view to improving the facilities available in the Leicester area. The questionnaire has been designed in the light of discussions with the Dean of Medicine at Leicester University, Professor Kilpatrick, the Department of Pharmacology and Therapeutics and the Regional Drug Information Service, and is distributed with official approval. The project is supervised by the University of Leicester's Primary Communications Research Centre.

To complete the questionnaire, I would like you to give factual details about your medical training, and to state how you use the various types of information about drugs that are available to you. The data obtained from the individual questionnaires will be treated as absolutely confidential; to ensure this, the questionnaire will be entirely anonymous.

For your convenience in completing the questionnaire, some of the questions have been supplied with a range of possible answers. In these cases, please tick the answer which approximates most closely to your own situation.

Thanking you for your co-operation,
Pat Hibberd.

1. Please state your
   - Medical Qualifications _____
   - Medical School _____
   - Year of Graduation from Medical School _____

2. Please state your position in the hospital

Consultant	☐	SHO	☐
Senior Registrar	☐	HO post registration	☐
Registrar	☐	HO pre registration	☐
SHMO	☐	Others - please state	
JHMO	☐	_____	

3. Which branch of medicine do you practise? _____

4. Please state as precisely as possible which sources of information you would use to check on the following when you are prescribing a drug with which you are less familiar.
   a) Indications _____
   b) Dose _____
   c) Strength _____
   d) Contraindications _____
   e) Adverse Effects _____
   f) Usefulness _____
   g) Alternative Drugs _____
   h) Drug Interactions _____

5. There are many sources from which doctors learn about new drugs. I am interested in knowing how useful you find these sources, firstly for getting to know about the existence of a drug, and secondly for getting to know about the usefulness of the drug. Please tick those that you find useful in each category.

	Useful for finding out about the existence of a drug	Useful for finding out about the usefulness of a drug
a) Articles in Medical Journals		
i) Subscription Journals		
British Medical Journal.....	☐	☐
The Lancet.....	☐	☐
New England Journal of Medicine.....	☐	☐
Journal of the American Medical Association.....	☐	☐
Journals concerned with your specialty - please state any you find particularly useful		
_____....	☐	☐
_____....	☐	☐
_____....	☐	☐
ii) Controlled Circulation Journals		
Hospital Update.....	☐	☐
World Medicine.....	☐	☐
British Journal of Hospital Medicine.	☐	☐
Others - please state any you find particularly useful		
_____....	☐	☐
_____....	☐	☐
b) Publications mainly concerned with Drug Information		
Drug and Therapeutics Bulletin.....	☐	☐
Adverse Drug Reaction Bulletin.....	☐	☐
Medical Letter.....	☐	☐
Rational Drug Therapy.....	☐	☐
Prescribers' Journal.....	☐	☐
British National Formulary.....	☐	☐
Bulletins from the Committee on Safety of Medicines.....	☐	☐
Others - please state		
_____....	☐	☐
_____....	☐	☐

5. continued

	Useful for finding out about the existence of a drug	Useful for finding out about the usefulness of a drug
c) Hospital Pharmacy		
Ward Pharmacist.....	☐	☐
Drug Information Centre.....	☐	☐
Hospital Pharmacy Department.....	☐	☐
d) Information from Drug Firms		
MIMS.....	☐	☐
Drug Firm Mail.....	☐	☐
Drug Firm Representatives.....	☐	☐
Advertisements in Medical Journals..	☐	☐
Local Drug Firm Meetings (excluding symposia).....	☐	☐
Data Sheets (including the ABPI Data Sheet Compendium).....	☐	☐
Others - please state		
_____....	☐	☐
_____....	☐	☐
e) Miscellaneous Sources		
Medical Libraries.....	☐	☐
Recommendations from Colleagues.....	☐	☐
Hospital Post Graduate Meetings.....	☐	☐
Others - please state		
_____....	☐	☐
_____....	☐	☐

6. Do you feel that you are able to obtain an unbiased assessment of a newly introduced drug ? YES ☐ NO ☐
If YES, what sources of information would you consult to obtain such an unbiased assessment ?

_____

If NO, why not ? _____

_____

7. Do you find that reports of clinical trials published in journals are a useful source of information about new drugs ? YES ☐ NO ☐
If NO, why do you find this ? _____

_____

_____

_____

8. On average, how many drug firm representatives try to see you each month

   - personally ?..... ☐
   - with other doctor ?..... ☐

9. How many of these representatives do you see ?

   - NONE..... ☐
   - SOME..... ☐
   - MOST..... ☐
   - ALL..... ☐

10. Do you think that you would lose an important source of information if you did not see any representatives ? YES ☐ NO ☐

11. On average, how much drug firm mail do you receive in the post each week ?

at HOME		at HOSPITAL	
1-5 items	☐	1-5 items	☐
6-10 items	☐	6-10 items	☐
11-15 items	☐	11-15 items	☐
more than 15 items	☐	more than 15 items	☐

12. Do you ever keep direct mail advertisements (EXCLUDING Data Sheets) for reference ? YES ☐ NO ☐

13. Do you ever keep Data Sheets ? YES ☐ NO ☐

14. Do you think that you would lose an important source of information if you did not receive any drug firm mail ? YES ☐ NO ☐

15. Have you ever written to a pharmaceutical firm for further information about a drug ? YES ☐ NO ☐

   If YES, a) do you write regularly for information ? YES ☐ NO ☐

   b) have you ever written for specific information YES ☐ NO ☐

16. Do you ever follow up references cited on drug advertisements ? YES ☐ NO ☐

   If YES, do you usually find that this information is useful ? YES ☐ NO ☐

17. Finally, in the future development of drug information systems, what information would you like to see available for each drug on the market ? Please tick any of the following and add any other pieces of information that you consider important.

- Approved Name..... ☐
- Indications..... ☐
- Dose..... ☐
- Strength..... ☐
- Route and Time of Administration..... ☐
- Contraindications..... ☐
- Special Precautions..... ☐
- Any Reported Adverse Reactions..... ☐
- Usefulness..... ☐
- Overdosage Treatment..... ☐
- Drug Interactions..... ☐
- Presentation (e.g. Tablet etc.)..... ☐
- Cost..... ☐
- Absorption and Distribution of the drug in blood and body tissues, and Excretion of the drug..... ☐

Others - please state

_____

_____

_____

_____

_____

_____

Thank you for completing the questionnaire. Please place it in the envelope provided and send by internal mail to the Post-Graduate Medical Librarian, who has kindly offered to collect them. In due course, I will provide a summary of the results of the investigation.

PLEASE RETURN THE COMPLETED QUESTIONNAIRE BY THE 31st MARCH 1977.

APPENDIX 2B

STUDIES OF THE USE OF DRUG INFORMATION SOURCES BY DOCTORS

Investigator *	Year	Area of Investigation	Sample Size	Method ‡
Caplow[1]	1951	Midwest doctors, U.S.	129	?
Gaffin[2]	1952	National, U.S.	500	PI
Caplow & Raymond[3]	1953	8 Midwest States, U.S.	182	PI
Coleman et al[4]	1954	4 Midwest Cities, U.S.	228	PI
Menzel & Katz[5]	1954	New England City, U.S.	33	PI
Gaffin[2]	1954	Wisconsin, U.S.	55	PI
Ferber & Wales[6]	1956	Chicago, U.S.	328	PI/D
Gaffin[2]	1957	National, U.S.	1,011	PI
Winick[7]	1958	Large City, U.S.	816	PI
Bauer[8]	1958	?	600	Q
Bursk[9]	1960	Massachusetts, U.S.	?	?
Wilson et al[10]	1963	Liverpool, U.K.	32	D
Sainsbury[11]	1966	National, U.K.	463	PI
Shaw & van Nevel 12	1966	University of Wisconsin, U.S.	144	Q
Henley et al[13]	1968	Iowa doctors, U.S.	?	?
Linn & Davis[14]	1970	Los Angeles, U.S.	131	Q
Becker et al[15,16]	1970	Mid-Atlantic States,U.S.	37	PI/Q
O'Keefe[17,18]	1970	6 Cities, N. Carolina, U.S.	283	Q
Eaton & Parish[19]	1970	National, U.K.	453	Q
Dunnell & Cartwright[20]	1972	?	325	Q
American Medical Association 21	1973	National, U.S.	96,950	Q
Applied Management Sciences 22	1973	National, U.S.	10,027	Q
Smith[23]	1973	West Washington State, U.S.	1,227	Q
Market Investigations (PA) Limited 24	1975	?	398	PI

* Numbers are for the references which follow

‡ PI = Personal Interview; Q = Questionnaire; D = Diary Method

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CHAPTER 3

THE INFORMATION CONTENT OF PUBLISHED REPORTS OF CLINICAL TRIALS

INTRODUCTION

The clinical, or therapeutic, trial occupies a position of importance in medical science today. This is a result of the legal requirement for a manufacturer to demonstrate that a new product is both safe and efficacious before it can be granted a Product Licence. Details of the legislation controlling this stage of drug development are included in Chapter 1.

The Medico-Pharmaceutical Forum's Working Party on Clinical Trials (1974) recommended that

> "editors of medical journals that publish clinical trials should accept that they have a considerable responsibility in guiding therapeutic opinion. Every effort should be made to ensure that phrases and definitions used are clearly understood....and that the trial is referred to an independent referee to ensure that it comes up to an acceptable standard."[1]

Several authors[2-4] have proposed various methods for assessing reports of clinical trials. Mahon and Daniel[2] suggested that the following criteria should be used to assess the adequacy of the trial:

a. presence of adequate controls, including effects of a placebo as well as standard therapy;
b. random allocation of treatment to each patient, to remove physician bias in assigning therapy;
c. objective evaluation of drug effects, including the double-blind method if it was possible;
d. statistical analyses of the results.

The double-blind technique requires that both the patient and the investigator are not informed about whether a patient is

taking the drug under investigation, or either a placebo or another active drug. Only those trials that include all of the above criteria were considered to be valid.

This method of assessment had been used by Reiffenstein et al[5] and Stimson.[6] Lionel and Hexheimer[3] felt that the approach was too "rough and ready". They proposed that a very comprehensive checklist could be used to assess the acceptability of clinical trial reports. The checklist was divided into sections which described the aim, the subjects taking part, details of drug administration, the methods, and the design and assessment of the trial. On this basis they decided on the overall acceptability of the trial report. This checklist may be very valuable to clinical pharmacologists but since some of the assessment is based on subjective criteria, it may be difficult for the non-specialist physician and the editor of a medical journal to use.

Roos[4] described a system for evaluating clinical trials suggested by Jonsson et al. It involved assigning a score to the various points that they considered important. For example, if the aim of the trial was well defined, poorly defined or not defined at all it scored two, one or no points respectively. Apart from the subjective division between a well defined and a poorly defined trial, the artificial differentials of two points and one point do not have any true meaning.

The object of the analysis described in this Chapter was to study the information that was actually contained in a sample of clinical trial reports. This was considered to be of value as the majority of hospital doctors use reports of trials to obtain information on new drugs (see Chapter 2).

METHODS

1. The Sample

All reports of clinical trials appearing in six general medical journals between January and June inclusive of the years 1960, 1965, 1970 and 1975 were selected for analysis. Trial reports were identified by the inclusion of the word "trial" in a paper. The journals were the British Medical Journal, The Lancet, the British Journal of Clinical Practice, the Clinical Trials Journal, Current Medical Research and Opinion and the Journal of International Medical Research. A sample of 259 clinical trial reports was produced.

2. Analysis of the Information Content

A checklist was prepared to assess whether certain items of information were included in the title, materials, methods, discussion and summary sections of each trial report (see Appendix 3A).

The title was expected to include the brand or generic name of the drug undergoing investigation and the disease that it was treating. The materials and methods sections were required to provide enough information to permit a different investigator to repeat the clinical trial. This included details of the number of patients taking part in the trial, the indications for which they were treated and other patient data e.g. age and sex etc. The methods required details of drug administration, the duration of treatment, the controls used and the method by which the results were measured to be mentioned.

The discussion was to include the criteria used to decide

on the dosage levels used in the trial, a statement about whether checks were made on patient compliance and an explanation of the reasons why the number of patients who started a trial was greater than the number that finished the course of treatment, if this was relevant.

Finally, the summary was expected to state the name of the trial drug (either brand or generic), the type of action that it possessed (e.g. antihypertensive etc.), the disease that it was treating, the number of patients taking part in the trial, the dosage schedules used, the duration of therapy, the design of the trial (e.g. double blind etc.), the results of the trial and whether or not the results were significant. The number of summaries that included the generic name of the trial drug at least once was also recorded.

To simplify the presentation of the data, if a particular item of information was either implicit in the text (e.g. oral contraceptives would be taken by women etc.) or not necessary to enable the trial to be repeated (e.g. checks on patient compliance when the drug was administered as an injection by either a doctor or a nurse), it was considered to have been mentioned. This was to avoid using three categories of results - one for data included, one for data that was not directly relevant to the trial and one for data that was not mentioned.

RESULTS

1. General Characteristics of the Sample

The number of trial reports appearing in each of the journals and the percentage of total articles that were devoted

to clinical trial reports are shown in Table 1 (see page 83).

The British Medical Journal and The Lancet published approximately the same percentage of reports of clinical trials to total articles, in each of the years studied. The remaining four journals devoted more space to publication of trial reports. The British Medical Journal and The Lancet have higher circulation figures (85,948 and 31,225 respectively in 1975[7]) than the British Journal of Clinical Practice (6,000[7]), the Clinical Trials Journal (10,000[7]), Current Medical Research and Opinion (6,000[7]) and the Journal of International Medical Research (5,870[7]). These two factors allowed the journals to be separated into two distinct categories, which were referred to as "high circulation journals" (i.e. the British Medical Journal and The Lancet) and "low circulation journals" (i.e. the British Journal of Clinical Practice, the Clinical Trials Journal, Current Medical Research and Opinion and the Journal of International Medical Research).

An increasing number of clinical trial reports were published between 1960 and 1975 in the low circulation journals ($P<0.001$). This was mainly due to the launching of the Clinical Trials Journal in 1964 and both Current Medical Research and Opinion and the Journal of International Medical Research in 1972.

The type of drug that was undergoing trial was recorded and classified using the therapeutic groups listed in the Personal and Social Services Statistics for England (1975) published by the Department of Health and Social Security. (Appendix3B lists these groups and the percentage of total prescriptions written for drugs in each therapeutic group, in 1975.) If a trial drug belonged to more than one category, the disease for which its value was being investigated was used to place it in a unique category. The results are shown in Table 2

TABLE 1

VOLUME OF SPACE OCCUPIED BY CLINICAL TRIAL REPORTS IN THE JOURNALS SELECTED FOR ANALYSIS

Journal	No. of C.T. * Reports	Total No. of Articles	$\frac{\text{C.T. Reports}}{\text{Total Articles}} \times 100$ %
British Medical Journal			
1960	14	562	2.5
1965	9	532	1.7
1970	17	548	3.1
1975	19	540	3.5
	56	2182	2.7
The Lancet			
1960	14	303	4.6
1965	13	383	3.4
1970	14	286	4.9
1975	15	291	5.2
	56	1263	4.4
British Journal of Clinical Practice			
1960	7	38	18.4
1965	10	30	33.3
1970	15	39	38.5
1975	18	37	48.7
	50	144	34.7
Clinical Trials Journal			
1965	7	18	38.9
1970	10	15	66.7
1975	4	4	100.0
	21	37	56.8
Current Medical Research and Opinion			
1975	30	58	51.7
Journal of International Medical Research			
1975	43	69	62.3

* C.T. = Clinical Trial

(see page 85). There was a significant difference in the type of drug undergoing trial reported in the high and low circulation journals ($P<0.01$).

The institution to which the author(s) of the papers belonged was recorded. This was either a hospital, a university, an academic (if a combination of authors from a hospital and university had written the paper), the pharmaceutical industry or general practice. If the authors belonged to more than one institution, and this was not a combination of a hospital and university, the data were classified as "others". The results are presented in Table 3 (see page 86).

The authors' addresses were used to determine the country in which the trials had been carried out, if no other indication was given in the report. Seventyfour percent of all trials were reported by authors in British institutions. The countries from which trials originated are shown in Table 4 (see page 87).

2. Information Content of the Clinical Trial Reports

The information contained in the various sections of the clinical trial report is shown in Table 5 (see page 88). There was very little difference in the information content of high and low circulation journals in all sections except the summary. High circulation journals were found to contain significantly more information in this section than low circulation journals ($P<0.01$).

The summary in both high and low circulation journals contained significantly more information in 1975 than in 1960 ($P<0.05$ and $P<0.01$ respectively).

TABLE 2

TYPE OF DRUG USED IN THE REPORTS OF CLINICAL TRIALS

Preparations acting on or affecting the:	High Circ. Journals %	Low Circ. Journals %	% of Prescriptions in 1975 (England)
Alimentary System	5	3	7
Cardiovascular System	18	13	12
Lower Respiratory System	4	4	10
Nervous System	24	40	27
Genito-Urinary System	2	4	1
Infections - Systemically	11	12	13
Metabolism	12	3	4
Nutrition and Blood	10	3	5
Rheumatic Diseases	1	8	4
Others	13	10	17

TABLE 3

THE INSTITUTIONS TO WHICH AUTHORS OF CLINICAL TRIAL REPORTS BELONGED

Institution	High Circulation Journals %	Low Circulation Journals %
Hospital	63	56
Academic	14	1
University	10	3
General Practice	3	14
Industry	-	7
Other	11	19

TABLE 4

COUNTRY OF ORIGIN OF CLINICAL TRIAL REPORTS

Country	High Circulation Journals %	Low Circulation Journals %
Australia	3	1
Belgium	-	2
Brazil	-	1
Britain	79	78
Britain/Holland	-	1
Canada	2	-
Cuba	1	-
Denmark	-	1
EEC Countries	1	-
Egypt/Holland	-	1
Eire	1	1
Fiji	1	-
Finland	1	1
France	-	2
Holland	3	1
India	1	1
Israel	-	1
Italy	-	2
Japan	-	1
Malta	-	1
Mexico	-	1
Nigeria	2	1
Norway	1	-
Pakistan	1	1
South Africa	1	-
Spain	1	-
Sweden	2	1
Switzerland	-	1
USA	2	1
Yugoslavia	-	1

TABLE 5

INFORMATION CONTENT OF REPORTS OF CLINICAL TRIALS

Items of Information Mentioned	High Circ. Journals %	Low Circ. Journals %
1. The Title		
Drug name	90	98
Disease name	94	73
2. Materials		
Subjects - healthy or patients	100	100
Number of subjects taking part	98	98
Age of subjects	75	78
Sex of subjects	75	71
Race of subjects	4	4
Disease diagnosis in subjects	97	89
Duration of disease	47	30
Presence/absence of other diseases	47	24
Other drugs being taken in addition to trial drug	39	26
Status of parameters of measurement at the start of the trial	53	51
3. Methods		
Presentation of the drug	83	79
Source of the drug	77	89
Daily dose	97	92
Frequency of administration	91	86
Route of administration	90	80
Timing of administration	51	33
Total duration of treatment	93	93
Use of controls	93	82
Subjective measurements	37	80
Objective measurements	65	56
Trials using Controls		
Single blind	4	5
Double blind	56	53
Between patient	57	49
Within patient	30	24
Random allocation of treatment	70	54
Use of matching dummies	78	70
Against placebo/standard therapy	57	48
4. Discussion		
How dosage levels were decided upon	50	48
Checks on patient compliance	40	19
Reasons for withdrawing patients (if relevant)	91	83
5. Summary		
Name of the trial drug	89	90
Type of action	36	17
Disease drug was treating	91	79
Number of patients on trial	81	74
Dosage schedules used	41	38
Duration of therapy	34	40
Design of trial	61	44
Results of the trial	94	76
Significance of the results	42	33
Generic name of the drug	89	75

The various categories are explained in Appendix A.

DISCUSSION

1. Problems of Checklist Design

By checking the presence or absence of particular items in a clinical trial report, the information content is assessed more objectively than by other methods. However, certain items, such as the status of the parameters of measurement at the start of the trial, require the observer to judge which parameters are relevant to the trial, and this involves some subjective assessment.

The items in the checklist included some points used by Lionel and Herxheimer[3] in the evaluation of clinical trial reports.

The journals used in this study were selected from those that were cited in a series of drug advertisements,[8] providing that they were published in the U.K., were non-specialist and were directed at the medical profession as a whole, rather than a specific group of doctors, e.g. general practitioners.

2. The General Characteristics

The conduct of clinical trials in the particular years that were studied were affected by changing legislation. In 1960, no legislation existed in the U.K., but by 1965 voluntary control of clinical trial procedure was operative. In 1970, the Medicines Act had been passed, but it was not implemented until 1971. The trials published in 1975 were probably conducted after this legislation was in force.

The increasing number of reports of clinical trials published in medical journals appears to have resulted from the increased demand and incentive, which has followed the

legislation. The demand has been created by the medical profession who use the reports to obtain information on new drugs (see Chapter 2). The incentive has resulted from authors who use the opportunity to carry out trials and publish articles as a method of career advancement and the pharmaceutical industry that can use the trial reports in a promotional way.

It was interesting to note that the trials investigating drugs which acted on the nervous system were more likely to be published in low circulation journals. Since the majority of these trials use subjective methods of assessment (often the "feeling" of the patient), a correspondingly higher proportion of results in low circulation journals used subjective assessment. It is possible that the two high circulation journals tended to publish reports using objective assessment, to give a more "scientific" image to the journal.

It was not surprising that the majority of the authors had hospital, university or academic addresses. This is because staff in these environments tend to have more facilities available and have more time for research.[9] Trials carried out in general practice are often "post-marketing trials" which are carried out once there are few or no legal restrictions on the supply of a product.

Since the journals studied were published in Britain, the majority of the trials were carried out in the U.K. Regulations governing the conduct of clinical trials in different countries can very considerably, as shown in Appendix 3C. It was not possible to investigate whether government regulations or editorial policy affected the information content of trials originating from different countries, as the regulations for some countries were not available.

3. The Information Content of Reports of Clinical Trials

It was surprising to discover that some trial reports did not include the name of the drug under investigation in the title of the article. Since the title is used to retrieve published articles from several information data bases (see Chapter 5, Appendix 5B), the absence of this information is difficult to understand.

The very low percentage of trial reports that mentioned the race of the subjects taking part in the trial indicated that it was not considered to be an important factor by the majority of trialists. However, racial differences can affect the response of a patient to a drug.[10] It is possible that the authors have assumed that their addresses indicate the country in which the trial was carried out, and that patients were always nationals of that particular country.

Trials also tended not to report whether checks were made on the compliance of patients in taking the medication that was prescribed for them (either the trial drug or a comparative drug or placebo). Boyd et al[11] reviewed the literature concerning drug defaulting (i.e. failing to comply with the directions of doctors in the self administration of medication) and found several studies reporting that between 80% and 90% of patients did not take their medication as directed. It is not clear whether these data were obtained in a hospital or general practice environment, although it would be expected that drugs provided to in-patients in hospitals would be taken.

The summary is perhaps the most widely read part of any paper, once the reader has decided from the title that the article is of interest to him. Hawkins[12] pointed out that it may be

reproduced throughout the world in many cases without the accompanying article. Therefore it should be brief and clear and mention essential points. Although the items chosen to estimate the information content of the summary do represent an opinion, a large percentage of articles failed to mention the type of action that a drug had, the dosage regimen used, the duration of therapy and whether or not the results of the trial were significant. High circulation journals tended to mention all of these points more often than low circulation journals.

It appears that certain items are not well reported in articles describing clinical trials, and there is no indication that there is any improvement when the data obtained from reports published in 1960 were compared with those published in 1975, with the exception of the summary section. However, the majority of the criteria assessed in this chapter were well satisfied by all journals.

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APPENDIX 3A

CHECKLIST TO ASSESS THE INFORMATION CONTENT OF PUBLISHED REPORTS OF CLINICAL TRIALS

Are the following items of information included ?

1. The Title:
   - a. the name of the drug undergoing trial; ☐
   - b. the disease that the drug is intended to treat. ☐

2. The Materials:
   - a. whether the trial subjects were healthy volunteers or patients; ☐
   - b. the number of subjects taking part in the trial; ☐
   - c. the age (or age range) of the trial subjects; ☐
   - d. the sex of the trial subjects; ☐
   - e. the race of the trial subjects; ☐
   - f. the diagnosis of the disease of the trial subjects; ☐
   - g. the duration (or range of duration) of the disease in the trial subjects; ☐
   - h. whether the trial subjects had other diseases, in addition to the disease being treated; ☐
   - i. whether the trial subjects took other forms of medication, in addition to the trial drug; ☐
   - j. the status of the parameters of measurement at the start of the trial, either for each subject, or the range of values for the trial subjects as a group. ☐

3. The Methods:
   - a. the presentation of the drug (i.e. tablet etc.); ☐
   - b. the source of the drug (e.g. manufacturer etc.); ☐
   - c. the daily dose taken by the trial subjects; ☐

d. the frequency of administration of the drug; ☐

e. the route of administration of the drug; ☐

f. the timing of drug administration (e.g. before meals etc.); ☐

g. the total duration of treatment with the trial drug; ☐

h. the use of controls (see below); ☐

i. the use of subjective measurement to assess the effect of the drug; ☐

j. the use of objective measurement to assess the effect of the drug; ☐

Trials Using Controls

The use of controls was assessed by the use of one or more of the following:

a. single blind trial - the patient does not know whether he is receiving the trial drug or some other treatment; ☐

b. double blind trial - neither the patient nor the patient is aware which treatment the patient is receiving; ☐

c. between patient - two groups of patients are compared, one group has received the trial drug and the other has received some other treatment. Usually an attempt to standardise patients(by matching for as many physical and social characteristics as possible) is made; ☐

d. within patient - the patient acts as his own control by taking both the trial drug and the other form of medication sequentially; ☐

e. random allocation of treatment to the various groups of patients taking part in the trial; ☐

f. use of matching dummies requires patients to be matched as carefully as possible for physical and social characteristics, and one group of patients usually takes a placebo, whilst the other takes the active trial drug; ☐

g. Against placebo or standard therapy requires the trial drug to be compared with either a pharmacologically inactive substance (placebo) or an active drug that is usually modified to have the same appearance as the trial drug. ☐

4. The Discussion:

a. how the dosage levels used by the trial subjects was decided upon; ☐

b. whether checks were made on the compliance of patients in the taking of their medication; ☐

c. reasons for withdrawing the patients from the trial (if this was done). ☐

5. The Summary:

a. the name of the trial drug; ☐

b. the type of action that the drug possessed (e.g. beta blocker, anti-convulsant); ☐

c. the disease that the drug was intended to treat; ☐

d. the number of patients on the trial; ☐

e. the dosage schedules used by the trial subjects; ☐

f. the duration of treatment with the trial drug; ☐

g. the design of the trial (i.e. the use of controls, or other attempts to measure patient response in an objective manner); ☐

h. the results of the trial; ☐

i. the significance of the results (or lack of significance); ☐

j. the use of the generic name of the drug. ☐

APPENDIX 3B

PERCENTAGE OF PRESCRIPTIONS - DISTRIBUTION BY THERAPEUTIC GROUP FOR 1975

PREPARATIONS ACTING ON OR AFFECTING:		%
The Alimentary System		7.2
01	Antacids and antispasmodics	3.3
02	Bitters, tonics and gastro-intestinal sedatives	1.5
03	Laxatives, puratives, evacuent enemas and suppositories, other preparations acting locally on the rectum and anti-infective agents acting locally on the gastro-intestinal tract	2.5
The Cardiovascular System and Diuretics		11.6
04	Preparations acting on the heart	2.8
05	Diuretics	4.6
06	Anti-hypertensives	2.1
07	Vasodilators, vasoconstrictors	1.7
08	Anticoagulents, and other preparations acting on the vascular system	0.4
The Lower Respiratory Tract		9.6
09	Expectorants and cough suppressants	5.8
10	Preparations relaxing bronchial spasm	3.0
11	Other preparations acting locally on the Lower Respiratory Tract, respiratory stimulants and others	0.8
The Nervous System		26.8
12	Addictive analgesics	0.2
13	Antipyretic analgesics	6.8
14	Hypnotics (barbiturate)	2.4
15	Hypnotics (non-barbiturate)	3.5
16	Tranquillisers	7.3
17	Antidepressants	2.8
18	Stimulants and appetite supressants	0.9
19	Anticonvulsants, preparations used in Parkinsonism, cholinergic and neuromuscular blocking drugs	1.4
20	Local anaesthetics and counter-irritants	0.8
21	Anti-emetics (other than preparations ofunadmixed hyoscine salts)	0.7
The Genito-Urinary System (22)		0.7
Infections - Systemically		13.1
23	Penicillins	5.9
24	Tetracyclines	3.3
25	Other antibiotics	1.5
26	Sulphonamides	0.4
27	Other anti-infective agents	1.9

PREPARATIONS ACTING ON OR AFFECTING:		%
Metabolism		4.2
28	Corticosteroids (systemic use)	0.8
29	Oestrogen-progestogen combinations	1.2
30	Other sex hormone preparations	0.7
31	Insulin and oral hypoglycaemics	0.7
32	Thyroid, anti thyroid and other preparations including hormones affecting metabolism	0.7
Nutrition and Blood		5.0
33	Iron and erythropoietic preparations	2.3
34	Vitamins and vitamin preparations	1.6
35	Other drugs affecting nutrition and blood	1.2
Rheumatic Diseases (36)		3.6
Allergic Reactions (37)		2.5
Ear, Nose and Oropharynx (38)		2.5
Eye (39)		1.4
Skin and Mucocutaneous Junctions		6.8
40	Anti-bacterial agents, fungicides	1.2
41	Corticosteroid preparations acting on the skin	3.6
42	Vehicles, sedatives, antiseptics and other preparations acting on the skin and muco-cutaneous junctions	2.0
Immunological Preparations (43)		0.4
Other Drugs and Preparations (44) including individually formulated preparations		2.0
Dressing and Appliances		2.6
45	Dressings	1.8
46	Appliances	0.5
47	Trusses	0.0
48	Hosiery	0.3

Source: Health and Social Service Statistics for England, 1976.

APPENDIX 3C

REGULATIONS AFFECTING THE CONDUCT OF CLINICAL TRIALS IN THE COUNTRIES FROM WHICH THE PUBLISHED REPORTS ORIGINATED

	System for Authorisation or Surveillance	Detailed Data Required by Authorities
Australia	approval necessary	++
Belgium	none	++
Brazil	none	none
Britain	approval necessary	++
Canada	approval necessary	++
Cuba	..	..
Denmark	notification necessary	++
EEC	none	none
Egypt	..	..
Eire	approval volutary	++
Fiji	..	..
Finland	notification necessary	++
France	notification necessary	++
Holland	notification necessary	++
India	approval necessary	++
Israel	approval necessary	++
Italy	none	none
Japan	notification necessary for some types of drug	none
Malta	..	..
Mexico	none	none
Nigeria	..	..
Norway	notification necessary	++
Pakistan	none	none
S. Africa	notification necessary	++
Spain	approval necessary	++
Sweden	notification necessary	++
Switzerland	none	none
USA	approval necessary	++
Yugoslavia	..	..

Source: International Federation of Pharmaceutical Manufacturers Associations, Legal and Practical Requirements for the Registration of Drugs (Medicinal Products) for Human Use, Zurich, 1975, p114.

Key .. denotes no information available

++ denotes information is required

CHAPTER 4

ADVERTISING BY THE PHARMACEUTICAL INDUSTRY AS A SOURCE OF INFORMATION ABOUT DRUGS

The pharmaceutical industry, unlike all other industries, cannot advertise the majority of its products directly to the consumer (the public). It is only permitted to advertise to members of the medical profession. Hence the medical profession is in the unique position of receiving large volumes of advertising, but it does not usually consume the products, and it does not foot the bill for the products that it directs others to use.

The amount of money spent by the pharmaceutical industry on the promotion of its products to the medical profession has always been a controversial subject. It has formed the basis of frequent argument and negotiation between the industry and the government in recent years. In 1976, the Department of Health announced that it was to reduce the allowable level of promotional expenditure from the existing level of 13.8% of its sales to the National Health Service (NHS) to 10% by 1979.[1] The possible effects of this reduction on advertising as a source of information is therefore of much interest.

Extent of Pharmaceutical Advertising

In 1975, £47.5 million was spent on advertising by the pharmaceutical industry in the UK.[2] The majority of this was directed at the 59,000 NHS doctors (general practitioners and full and part-time hospital doctors), which was equivalent to about £800 per doctor. Representatives accounted for about 50% of this cost,

journal advertising for 20-25% and the remainder was spent on direct mail, sponsored meetings, courses, film shows etc.[3] Several studies have reported the extent of contact that the industry has with doctors through representatives, direct mail and journal advertisements.

1. Representatives

A recent report on the Continuing Education of Doctors in Medicinal Therapeutics noted that

> "many doctors consider that their contacts with the pharmaceutical industry, often through representatives, are their most valuable source of continuing education in therapeutics." [4]

The approximately 150 UK based pharmaceutical firms employ some 3,000 medical representatives whose primary function is to communicate medical information about drugs to the 25,000 general practitioners and 34,000 full or part-time NHS hospital practitioners and the 14,000 pharmacists.[5]

Sainsbury[6] found that 65% of a sample of general practitioners in 1966 saw more than five representatives per month. Eaton and Parish[7] reported that almost all of the general practitioners that they surveyed in 1970 saw at least one representative per week. Hospital doctors were found to see considerably fewer representatives (see Chapter 2).

2. Direct Mail

The amount of direct mail received by general practitioners seems to have decreased dramatically. Sainsbury[6] reported that 91% of his respondents estimated that they received over 20 items per week, in 1966. Stimson[8] collected direct mail advertisements sent to 13 general practitioners in different weeks in 1974 and 1975 and found that, on average, each doctor received 7.5 items per week. Since Sainsbury's respondents may have exaggerated

the amount that they received, and the general practitioners in Stimson's study may not have provided all the advertisements that they were sent, the difference in the amount of mail received may be smaller than it initially appears. Hospital doctors (with the exception of clinical assistants) estimated that they usually received between 1-5 items per week both at home and at the hospital (see Chapter 2). No comparison between the amount of direct mail received by hospital doctors and general practitioners was made, because reductions in allowable promotional expenditure were announced after Stimson's study had been carried out, and therefore the amount received by general practitioners since 1975 may have decreased.

3. Journal Advertisements

It is not possible to open most medical journals without committing oneself to at least some of the advertisements, and hence Hamilton[9] considered that readership figures alone gave a reasonable indication of the exposure to this type of promotion. He found that 92% of a sample of general practitioners read the British Medical Journal.

Stimson[8] studied the maximum exposure of the average general practitioner to journal advertisements by calculating the average contents of the 36 issues of controlled circulation journals (i.e. unsolicited and distributed without a subscription fee) and six issues of subscription journals that a general practitioner would be likely to receive each month. The subscription journals included the British Medical Journal, the Practitioner, and the Journal of the Royal College of General Practitioners. To enable a comparison to be made with the number of advertisements appearing in two controlled circulation journals received by hospital doctors,

Hospital Update and the British Journal of Hospital Medicine, and two general subscription journals used by hospital doctors to learn about new drugs - British Medical Journal and The Lancet (see Chapter 2), data were calculated using Stimson's criteria for all issues of these journals appearing in 1977. In addition, data were calculated for all issues of the general practitioners subscription journals appearing in 1977. The results are shown in Table 1, (see page 104).

Several differences were observed:

a. controlled circulation periodicals contain fewer pages per issue than subscription periodicals;

b. although the total space occupied by advertisements is approximately the same for each category of journal, the space occupied by drug advertisements (as opposed to classified advertisements) in the controlled circulation journals is considerably higher than in the subscription journals;

c. controlled circulation journals directed at hospital doctors contain slightly fewer drug advertisement pages per issue than those directed at general practitioners;

d. slightly fewer drug advertisements appear in the general practitioner subscription journals in 1977 than in 1974/1975.

This last observation is of particular interest since the effects of the government's reduction in allowable promotional expenditure on journal advertising can be gauged. The exact magnitude of this reduction can be more reliably made by comparing the amount of space occupied by advertisements in specific journals before and after the announcement was made.

TABLE 1

AVERAGE CONTENTS OF PERIODICALS PER ISSUE

Average Contents	October 1974-March 1975 * Controlled Circulation Journals (G.P.)	Subscription Journals (G.P.)	January 1977-December 1977 Subscription Journals (G.P.)	Subscription Journals (Hospital)	Controlled Circulation Journals (Hospital)
Number of pages	51	120	129	114	84
Percentage of pages as					
- drug advertisements	42	23	19	15	36
- other advertisements	4	23	26	33	7
Number of different drugs advertised	34	27	21	14	26
Sample Size	200	39	76	104	24

* Source: Stimson[8]

(However, this assumes that no other factors affected the reduction.) Morgan et al[10] reported the percentage of space occupied by drug advertisements in selected medical journals in 1975. Table 2 shows these data and compares them with data calculated for the 1977 issues of the same journals (see page 106).

Number of Different Drugs Advertised

No data are available which state the number of different drugs advertised to doctors each month by representatives. Stimson[8] found that approximately 40 different drugs per month were advertised in the direct mail received by a sample of general practitioners in 1974 and 1975.

The total number of different drugs advertised in selected journals in 1977 are shown in Table 3 (see page 106) together with the percentage of the drugs advertised exclusively in each journal (i.e. did not appear in any of the other journals listed). On average, about 20% of the drug advertisements were exclusive to each journal. The remaining 80% of drugs were advertised in more than one journal. The extent of overlap can be considered by applying the formula:

$$\text{overlap} = \frac{\text{total number of drugs which were advertised in both of the journals being considered}}{\text{total number of different drugs advertised in both of the journals}}$$

and expressing the result as a percentage. The overlap between selected journals is shown in Table 4 (see page 107). The British Journal of Hospital Medicine and Hospital Update had the largest number of drug advertisements in common in 1977.

TABLE 2

PERCENTAGE OF SPACE DEVOTED TO DRUG ADVERTISEMENTS IN SELECTED JOURNALS

Journal	1975 study* %	1977 study %
British Medical Journal	22	19
The Lancet	14	9
British Journal of Hospital Medicine	38	35

* Source: Morgan et al[10]

TABLE 3

NUMBER OF DIFFERENT DRUGS ADVERTISED IN SELECTED JOURNALS IN 1977

Journal	Total No. Different Drugs	Drugs advertised exclusively in each Journal No.	%
British Medical Journal	130	41	32
The Lancet	49	5	10
British Journal of Hospital Medicine	87	16	18
Hospital Update	57	11	19
Journal of the Royal College of General Practitioners	32	6	19
The Practitioner	72	14	19

TABLE 4

OVERLAP OF DRUG ADVERTISEMENTS BETWEEN SELECTED JOURNALS IN 1977

Journals	Overlap %
British Medical Journal and The Lancet	27
British Medical Journal and British Journal of Hospital Medicine	32
British Medical Journal and the Practitioner	31
The Lancet and British Journal of Hospital Medicine	35
British Journal of Hospital Medicine and Hospital Update	40

Control of Drug Advertising

Prescription drug advertising is strictly controlled by the 1968 Medicines Act, and is discussed in detail in Chapter 1. In addition to the legal requirements, the majority of pharmaceutical firms follow a very strict code of practice laid down by the Association of the British Pharmaceutical Industry (ABPI). Member companies are required to adhere to this voluntary code, as a condition of membership. The code aims to

> "secure the universal acceptance and adoption of high standards of conduct in the marketing of medical products designed for use under medical supervision." 11

The code requires that representatives must:

1. be thoroughly trained and possess sufficient knowledge to present information on their own company's products in an efficient manner;
2. maintain a high standard of ethical conduct in the carrying out of their duties;
3. not use any inducement or subterfuge to gain an interview;
4. observe the wishes of any individual doctor, or the arrangements in force in any particular establishment, so as not to cause inconvenience;
5. take adequate precautions to ensure the security of medical products in their possession;
6. not use the telephone to provide information to any doctor, unless a specific arrangement to do so has been made.

The ABPI is hoping to bring out a new code of practice in 1978, and this is expected to require new representatives to pass an approved examination and to state how often a representative

may visit a doctor in any twelve month period.[12]

The regulations which affect printed promotional material are divided into two sections - those attempting to provide enough information to enable a member of the medical profession to reach a decision for prescribing, and those attempting to remind doctors of the availability and main indication of the product. The first type of advertisement must list:

1. the active ingredients, using approved or other non-proprietary names, contained in each unit dose;
2. recommended dosage, method of use and route of administration;
3. side effects, precautions and contraindications; of the product in the recommended dosage;
4. a statement that additional information is available on request;
5. the company name and address.

Reminder advertisements and those where it is

> "demonstratably and obviously impracticable to display legibly and full information" 11

require as a minimum:

1. the approved or other non-proprietary names of the active ingredients;
2. a statement that full prescribing information is available;
3. the company name and address.

The basic cost of the product to the NHS must be given in all promotional literature

> "except where references to this cost would clearly be inappropriate". 11

As can be seen from the above extracts from the code, several of the items it controls can be subject to many

interpretations and hence there is a fair amount of flexibility in the minimum information required in the various forms of promotion. A comparison of legal and voluntary requirements for printed promotional material, and the information that hospital doctors would like to have available for each marketed drug is shown in Table 5 (see page 111). It appears that several items concerning product use are not required to be mentioned.

Information Content of the Various Forms of Promotion

Various authors have attempted to assess the information provided by representatives, direct mail and journal advertisements.

1. Representatives

Hemminki[13] attempted to assess the information provided by medical representatives to a group of Finnish hospital doctors. The method included recruiting several doctors who silently observed the communication process and then completed a questionnaire concerning the information provided. The information that was spontaneously provided is shown in Table 6 (see page 112).

It was noted that 9% of the representatives did not state the indications of the product being promoted. It appears that the information that does not enhance the image of a company's product is provided considerably less often than information that mentions positive attributes of a product (i.e. its indications). Although the study itself had several possible sources of error including the inability of observers to remember details of the presentation and observer bias, some attempt to reduce these errors was made. For all presentations,

TABLE 5

LEGAL AND VOLUNTARY REQUIREMENTS FOR PRINTED PROMOTIONAL MATERIAL

Information that Hospital Doctors would like to have available for each marketed drug *	Information Provided By: Data Sheets (Medicines Act) ‡	ABPI Code of Practice Prescribing Information in Advertisements	Reminder Advertisements
Approved name	✓	✓	✓
Indications	✓	-	-
Dose	✓	✓	-
Strength	✓	✓	-
Route and time of administration	✓	✓	-
Contraindications	✓	✓	-
Special precautions	✓	✓	-
Adverse reactions	✓	-	-
Efficacy	-	-	-
Overdosage treatment	✓	-	-
Drug interactions	-	-	-
Presentation	✓	-	-
Cost	-	-	-
Absorption, distribution and excretion of the drug	-	-	-
(Side effects)	✓	✓	-

* See Chapter 2

‡ See Chapter 1

TABLE 6

INFORMATION PROVIDED SPONTANEOUSLY BY A SAMPLE OF REPRESENTATIVES IN PRESENTATIONS TO A GROUP OF FINNISH HOSPITAL DOCTORS

Item	% of representatives mentioning item
Indications	91
Generic Name	78
Price	35
Side effects	29
Contraindications (if relevant)	27
Competitive drugs	70
Alternative forms of therapy	4
Reference to a Finnish doctor with a positive attitude towards the drug	30
Reference to a Finnish doctor doing trials with the drug	22

Source: Hemminki[13]

two different observers completed questionnaires concerning the information provided and in 83% of the cases, the observers provided the same answers. Hemminiki[14] reported that drug firms in Finland regard "detailing" more as a sales activity than a public relations exercise and that this trend towards selling has gained more importance in the recent years.

It is not possible to state whether information provided by representatives in the U.K. would be similar to that provided by Finnish representatives for several reasons. Firstly, the legal and voluntary regulations affecting the provision of information by representatives may differ. Secondly, although a trend towards selling was reported by Banks et al[15] in 1964, there are no recent data to suggest that it has continued. Thirdly, behaviour of representatives who "detail" to hospital doctors may be different from those who "detail" to general practitioners. Information staff in 40 pharmaceutical firms in the U.K. were asked whether the techniques of sales promotion were the same for hospital doctors and general practitioners (see Chapter 5). The results are shown in Table 7 (see page 114). The majority of the respondents were only aware of promotional methods used by representatives, which in itself is an interesting result.

The only analyses of the information provided by representatives in the U.K. were reported by Sainsbury[6] and the Office of Health Economics[16] (which reported a survey carried out by Market Investigations (PA)Limited). Sainsbury found that 51% of his respondents had felt that there were instances of insufficient knowledge, 58% stated that side effects had sometimes been underplayed and 62% felt that there had been instances of a representative claiming more indications for a

TABLE 7

MEDICAL REPRESENTATIVES AS PROVIDERS OF INFORMATION

Factors affecting Provision of Information	Firms No.	Firms %
Type of Doctor Visited		
All representatives visit both hospital doctors and G.P.s	12	30
A separate group of representatives visit teaching hospitals, all others visit hospital doctors (non-teaching)	11	27
A separate group of representatives visit hospital doctors, all others visit G.P.s only	11	27
Did not know	6	15
Type of Information Provided to G.P.s and Hospital Doctors		
Information is the same	10	25
Information differs (usually more detailed for hospital doctors)	18	45
Did not know	12	30

product than was justified. It was interesting to note that the survey carried out by Market Investigations (PA) Limited produced rather different results. Sixtynine percent of their respondents felt that the thoroughness of the information provided by representatives fell precisely midway between the extremes of being too much and too little. Seventytwo percent felt that the descriptions of products were more likely to be accurate than distorted, and 85% felt that representatives were more likely to be well informed than poorly informed. The very different conclusions about the quality of information provided by representatives reported in the two studies were attributed to the difference in wording of the questions asked, the Sainsbury study leading doctors to offer a critical answer, and the second study asked "a more neutral series of questions".[16] Unfortunately the exact questions asked in this survey were not quoted. Another explanation offered was a dramatic improvement in the calibre and training of representatives in the ten years between the two studies.

2. Direct Mail

Although both Stimson[8] and Wilson[18] analysed the information content of direct mail advertisements, the results were not presented independently of the information content of journal advertisements, and therefore both will be discussed in the next section.

3. Journal Advertisements

Several authors have analysed the information contained in periodical advertisements. Stimson[17] studied the information content of a sample of drug advertisements appearing in subscription and controlled circulation journals that the majority of general practitioners would have received in 1974

and 1975. Morgan et al[10] reported the information content of advertisements appearing in the British Medical Journal, The Lancet, World Medicine, Teach In and the British Journal of Hospital Medicine. (World Medicine and Teach In are both controlled circulation journals sent to general practitioners.) Their results are compared in Table 8 (see page 117). The major conclusion reached by both groups of authors was that journal advertisements rarely contain information that is of use for prescribing. Stimson noted that 68% of all drugs advertised had been marketed within five years of the date of his analysis. In addition, the brand name was found to appear between three and four times more often than the approved name, and was, on average, seven times larger than the approved name. The total absence of the approved name in 8% of the advertisements was in direct conflict with the requirements of the ABPI code of practice.[19] Wilson[18] in a study of advertisements received by a general practitioner in 1968 found that 3% of the advertisements (direct mail and periodicals) did not name the active constituents of the preparation.

Stimson[20] found that 35% of the periodical advertisements that he studied gave references for product claims. This is higher than the 20% reported by Wilson[18] but lower than the 57% of advertisements that included references appearing in British periodicals analysed by Morgan et al[10]. The references were given in a style similar to that found in professional journals, and should enable the reader to check on the claims made by the advertisement. Stimson used the lists provided by several different types of medical library to assess the availability of the references quoted. Twentysix percent of the references were not available in any of the libraries chosen.

TABLE 8

INFORMATION CONTAINED IN DRUG ADVERTISEMENTS IN SELECTED JOURNALS

Items of Information	G.P. Journals* %	British Medical Journal‡ %	The Lancet‡ %	World Medicine‡ %	Teach In‡ %	British Journal of Hospital Medicine‡ %
Active ingredients	43	..	..	..	..	..
Approved name	..	99	99	98	99	97
Recommended dose	14	..	..	..	..	..
Cost	6	3	2	2	-	7
Contraindications	4	9	8	3	3	4
Side effects	4	..	..	..	..	..
Adverse effects: principal	..	6	6	3	3	5
full list	..	-	-	3	-	1
none mentioned	..	85	91	94	94	88
Special precautions	3	..	..	..	..	..
Interactions	..	-	-	2	-	-
Mode of action - pharmacological	..	13	13	7	14	6
Absorption	..	3	4	-	4	3
Distribution	..	2	3	-	-	-
Metabolism	..	-	-	-	1	-
Excretion	..	1	2	-	-	1

* Source: Stimson[17] ‡ Source: Morgan et al[10]

Key .. denotes information not measured, - denotes information absent

Morgan et al noted that references to data in file, unpublished data and quotations from symposia proceedings were prominent sources, and considered these to be unacceptable.

Stimson also reported a rather disturbing result,

> "We found some inconsistency between drug companies' claims and the original text of the references, and quotations in advertisements were occasionally presented in a manner which tended to change the meaning of the original text. Sometimes separate quotations were linked together as if they had been consecutive in the original and simply shortened for convenience.....It is hard to escape the conclusion that references are included in order to give a respectable scientific appearance to the advertisement rather than for their scientific usefulness." 19

Other Issues Affecting Drug Advertising

A simple analysis of the information content does not take into account the message of the drug advertisement and the overall image that it portrays. Wilson[18] reported that 34% of the advertisements he studied had a "rational" basis, using his personal judgement. Several authors have studied various types of irrationality in drug advertisements.

Smith and Visconti[21] separated the type of appeals appearing in drug advertisements into two categories - "rational" and "non-rational". The classification that they used is shown in Table 9 (see page 119). Hemminki[22] adapted this classification in a study of appeals used in drug advertisements in two leading Finnish medical journals in three six month periods during the years 1959, 1965 and 1971. She found that the text in 79% of the advertisements included product related appeals. The three main appeals used in the picture of psychotropic drug advertisements were curiosity (46%), empathy (27%) and clinical (20%). Smith and Griffin[23] analysed a sample of advertisements

TABLE 9

APPEALS USED IN PHARMACEUTICAL ADVERTISING

Rational	Non-rational
Product related	- empathy
- economy	- humour
- innovation	- sex
- differentiation	- curiosity
- mode of action or use	- unusual illustration (non-clinical)
	- ego-gratifying
Physician related	
- approval of peers	
- therapeutic aid to physician	
Clinical Use related	
- dependability	
- safety	
- clinical illustration	
- reminder	
- patient response	
Manufacturer related	

Source: Smith and Visconti[21]

appearing in 60 American medical journals in 1974. They found that 79% of the appeals used in psychotropic drug advertisements were "rational", but that male patients were more often associated with the use of "rational" appeals than female patients. The drawback of all these studies is the subjective nature of several of the categories defining rational and non-rational appeals, which would make it difficult for the study to be repeated.

Mant and Darroch[24] used content analysis techniques to study drug advertisements which appeared between 1969 and 1972 in two major Australian journals. They found that a greater use of female (than male) models in psychotropic drug advertisements. Prather and Fidell[25] confirmed this result in a study of drug advertisements appearing in two American medical journals between the years 1968 and 1972. They also noticed that women tended to be portrayed as suffering primarily from emotional illnesses, whereas men tended to be shown as suffering from organic illnesses. Stimson[26] reported a similar trend in British psychotropic drug advertising.

It is not known, however, whether sex stereotyping in psychotropic drug advertisements affects the information that the doctor obtains from the advertisement. The majority of the researchers quoted above have been concerned about the rather limited view of women portrayed in the advertisements.

Another group of patients that have been portrayed in a rather negative way in drug advertisements are the elderly.[27]

Use of Drug Advertising as a Source of Information

Smith[28] has recently reviewed the numerous studies reporting the use of drug advertising by American physicians. As there are

many differences in legal requirements and the amount spent on promotion etc. between the U.S. and U.K., these studies will not be reviewed in this chapter.

Five British studies have reported the use of drug advertising as a source of information by general practitioners. Wilson et al[29] in 1962 found that 23% of a sample of general practitioners would use drug firm promotions to obtain information on drugs. No attempt was made to separate the various forms of promotion. This result can be directly compared with the use of drug firm literature, representatives or meetings by 90% of a sample of general practitioners reported by Dunnell and Cartwright.[30] The reason for this very large difference is probably related to the actual questions asked. Wilson et al asked general practitioners which sources they used for "therapeutic" information, whereas Dunnell and Cartwright asked their respondents about the sources of information used to learn about new drugs. The survey reported by Market Investigations (PA) Limited[16] discovered that general practitioners considered that representatives were the most important source of information about new medicines, but MIMS was considered the most important for learning about established medicines.

Both Sainsbury[6] and Eaton and Parish[7] asked almost identical questions of general practitioners in 1966 and 1970 concerning the use of promotional material for learning about the existence and usefulness of a new drug. Their results are shown in Table 10 (see page 122). In addition, the results obtained from the survey of hospital doctors reported in Chapter 2 is included so that direct comparisons can be made. It appears that hospital doctors consider the representative as a much less

TABLE 10

USE OF DRUG ADVERTISING AS A SOURCE OF INFORMATION ABOUT NEW DRUGS

Respondents using Source	1966 - G.P.s* E %	1966 - G.P.s* U %	1970 - G.P.s‡ E %	1970 - G.P.s‡ U %	1977 - Hospital Doctors* E %	1977 - Hospital Doctors* U %
Representatives	78	61	90	51	55	42
MIMS	67	50	85	44	85	52
Periodical advertisements	53	19	62	17	39	12
Drug company literature	52	23	53	7	51	24
Drug firm sponsored meetings	37	33	65	44	27	21

* Source: Sainsbury[6]

‡ Source: Eaton and Parish[7]

* See Chapter 2 (Questionnaire Respondents only)

Key E refers to sources used to find out about the existence of a new drug

U refers to sources used to find out about the usefulness of a new drug

important source for learning about the existence and usefulness of a new product than their general practitioner colleagues. MIMS seems to have increased in importance between 1966 and 1970, and is used heavily by hospital doctors to find out about the existence of a new drug. Drug company literature is considered to be of about the same importance by all the studies, despite the reduction in volume of direct mail advertising between 1966 and 1975. Hospital doctors appear to receive less than their general practitioner colleagues, but do not consider this form of promotion to be of less importance. Periodical advertisements are a much more important source to general practitioners than hospital doctors. Sponsored meetings seem to be very important to doctors in the 1970 study, but, in general, are more important to general practitioners than hospital doctors.

Williamson[31] reported a study of the use of various sources of information about drugs and compared this with preconceived views of "therapeutic risk" associated with the prescribing of various classes of drugs. His results are shown in Table 11 (see page 124).

It appears that the lower the "therapeutic risk" of a particular drug, the greater the influence that promotional resources have on a decision to adopt a new drug. Conversely, products having a greater "therapeutic risk" were much less likely to be adopted without reference to a source provided by the medical profession.

In summary, it appears that drug advertising is a very important source of information about drugs, in particular for learning about the existence of new products. It appears

TABLE 11

SOURCES OF INFORMATION USED IN DECISIONS TO ADOPT NEW DRUGS

Source	Therapeutic Risk High %	Medium %	Low %
Representatives	25	31	39
Mailings	14	17	19
Journals	19	8	9
Colleagues	12	14	8
Consultants	18	8	4
Other sources	12	22	21
Percent of professional sources used	49	30	21

Source: Adapted from Williamson[31]

that the information provided by many of these sources is not entirely adequate, but the new code of practice from the ABPI may improve the quality of information in promotional material. No attempt to assess whether or not advertising is misleading was made because of the subjective nature of this concept. The effect of the government's decision to disallow promotional expenditure in excess of 10% of the value of sales to the NHS seems, as yet, to have had little effect on the number of advertisements appearing in medical journals.

The government appeared to recognise that restrictions on the promotional expenditure might cause several subscription and controlled circulation journals to collapse, as it did consider offering special protection to a selected few medical journals, by exempting the cost of advertising in these journals from the cuts. However, as a result of consultation which was unanimously against this proposal, the suggestion was dropped by the government.

Perhaps the major reason for the success of promotional material as a source of information about drugs is its easy availability and the lack of any totally comprehensive source of drug information.

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CHAPTER 5

PROVISION OF DRUG INFORMATION BY INFORMATION STAFF IN THE PHARMACEUTICAL INDUSTRY

INTRODUCTION

The pharmaceutical industry is a highly competitive research-based industry requiring efficient provision of information for its successful survival. This need for internal information has led to the formation and staffing of departments specialising in literature searching and information. Most companies extend the use of this department to members of the medical profession. Buckland pointed out that

> "drug information centres in industry have access to all the detailed knowledge accumulated from the time the drug was first developed; they have the key to information in the published literature, the knowledge of unpublished documentation, records of usage in unusual circumstances and, very important access to relevant experts." 1

As the majority of hospital doctors use the information available from the industry at some stage in their medical career (see Chapter 2), a study to investigate the provision of information by the industry was carried out during February, March and April of 1978.

METHOD

1. The Sample

A sample of 40 pharmaceutical firms was chosen for the interview survey. Thirtyeight (95%) had placed an advertisement

in either the British Medical Journal or the British Journal of Hospital Medicine in 1977, and were therefore likely to be actively providing information on their own products during the interview period. Although 57 firms fulfilled this criterion, the 38 were selected as shown in Table 1. Firms which are subsidiaries of other companies were not included if they did not provide information independently of their parent company.

An additional two firms were chosen from the remaining 55 companies contributing to the 1978 Association of the British Pharmaceutical Industry (ABPI) Data Sheet Compendium.

TABLE 1

SAMPLE OF PHARMACEUTICAL FIRMS APPROACHED FOR INTERVIEW

Number of advertisement pages in the 1977 issues of the British Medical Journal and British Journal of Hospital Medicine	Number of Firms	Firms approached for interview	
		No.	% in each category
None	55	2	4
1 -5	15	4	27
6 -11	12	6	50
12-23	10	8	80
more than 23	20	20	100
Total	112*	40	35

* This total refers to all companies contributing to the 1978 ABPI Data Sheet Compendium.

It was decided to limit the study to firms that were members of the ABPI for two reasons. Firstly, the ABPI represents the majority of the industry and secondly, ABPI members adhere to a code of practice and therefore are more uniform in their conduct. The firms included in this survey list significantly more products in the compendium than those not selected ($P<0.001$).

Each firm's contribution to the compendium either lists all of its products or those currently being promoted. Each different entry was taken to represent one product.

2. The Interview

The interview contained 28 questions which fell into well defined sections (see Appendix 5A).

The interview method was used because it allowed the interviewer to explain the motives behind any questions that the respondent considered sensitive. Initially, the respondents were asked to provide basic details about the information department (or equivalent) including the number of staff employed, the number of products for which the department was responsible and the qualifications held by the staff who answered enquiries. This was followed by questions concerning the gathering of information. This included access to "information systems" which were defined as any resource used for current awareness, i.e. information data bases that can be searched using computer retrieval facilities, indexing and abstracting publications. Provision of information was also assessed in several hypothetical instances.

The interview continued with questions about the hours

that information staff could be contacted, the number of enquiries received in the previous week and which information requests were most common. The efficiency of the service was judged by asking how quickly written and telephoned requests would be answered (assuming that telephoned requests could not be answered immediately).

Two questions were asked about the role of information departments in the functioning of the company. This was followed by several questions to determine the respondent's opinions of drug information centres in the National Health Service (NHS).

Finally the respondent was asked about the effect of commercial bias on the provision of information.

(A question was included to determine whether techniques of sales promotion were the same for general practitioners and hospital doctors, but the results of this question are discussed in Chapter 4.)

The interview took about half an hour, or longer if the respondent was particularly interested and enlarged on any of the points made.

RESULTS

1. The Response

All 40 of the firms approached co-operated, although two were unable to arrange an interview due to staff shortage. Staff from both of these firms filled in a questionnaire which contained exactly the same questions that were asked during the interview, and the data were included in the analysis.

2. Nationality of the Parent Company of the Firms included in the Survey

Seventyseven percent of the firms were owned by companies based outside the U.K. as shown in Table 2.

TABLE 2

NATIONALITY OF THE PARENT COMPANY OF THE FIRMS VISITED DURING THE INVESTIGATION

Nationality	Firms No.	%
British	9	23
American	13	33
German	4	10
Swiss	3	8
French	3	8
Dutch	2	5
Swedish	2	5
Other Western European	4	10

3. General Characteristics of the Information Department (or its equivalent)

Eightyeight percent (35) of the firms had a specific medical or drug information department which dealt with enquiries from the medical profession. The remaining five firms employed staff who answered enquiries, although there was no formalised department for this purpose. In two cases, information work was carried out in other departments, one in research and development, the other in sales promotion and

marketing. These five firms were all subsidiaries of companies based outside the United Kingdom.

The number and qualifications of information staff answering enquiries are shown in Table 3 (see page 134). To protect the identity of any particular firm, departments employing more than eight members of staff have been combined in one category. In all cases, secretaries employed in information departments have been omitted, because they did not answer enquiries made by members of the medical profession. A formal academic qualification was defined as a minimum of a B.Sc. or B.A. degree (or its equivalent), or a paramedical qualification. Membership of the Pharmaceutical Society of Great Britain (MPS) is awarded to pharmacists who have completed a year of recognised supervision, after obtaining their first degree in pharmacy.

Ninety percent of the staff held a formal academic qualification. In 33% of the firms, at least one medically qualified member of staff answered enquiries from the medical profession and 58% of the firms employed at least one registered pharmacist (MPS) for this purpose.

Information units in British firms tended to employ more staff than non-U.K. based firms. Fiftyseven percent of all firms employed less than four staff in information work and all but two of these firms were owned outside the U.K. The remaining 43% of firms employed four or more information staff and these firms were either British, American or Swiss based companies. A higher proportion of staff in British firms held medical or pharmacy qualifications.

Thirty percent of the departments were staffed by

information specialists equally able to answer any question. A further 45% of departments employed staff who were specialists in particular products or diseases, or created a distinction in the ability of staff to answer enquiries on the basis of qualifications or experience. The remaining 25% of departments had one member of staff. As would be expected specialisation tended to occur as the number of staff in the department increased ($P<0.05$), although departments employing two, three or four staff were equally divided between specialisation and non-specialisation.

TABLE 3

NUMBER AND QUALIFICATIONS OF INFORMATION STAFF

Number of staff in the Department	Number of Firms	MB BS or MB ChB	PhD	MPS	MSc	BSc	Para Medical Qualif.	No Formal Qualif.	Total No. of Staff
One	10	1	1	2		3	2	1	10
Two	7	2	1	6		2		3	14
Three	6	2		9	2	4		1	18
Four	8	5	1	8	4	14			32
Five	2	2	1	2	1	1	1	2	10
Six	2			2		8	1	1	12
Seven	2	1		3	5			5	14
Eight									
more than eight	3	8		8	2	17		2	37
Total	21		4	40	14	49	4	15	147
% of Total	14		3	27	10	33	3	10	100

All information staff were responsible for provision of information within their own company. This usually included the scanning of literature, production of current awareness bulletins and provision of a back-up information service for other company staff involved in marketing (including medical representatives), product registration and, occasionally, research and development. (Information for research and development was often carried out by the research scientists themselves under guidance of separate information staff, and in some cases, by separate departments set up entirely for this purpose.) In addition, all information staff answered enquiries from the medical profession.

Staff in 80% of the information departments were involved in the training of their own company's medical representatives. Other activities carried out by information staff are shown in Table 4 (see page 136). It is possible that these data are incomplete, but the main additional duties are probably included.

The number of products (i.e. number of therapeutic compounds having different indications) marketed by the 40 firms that participated in this study varied considerably. The distribution is shown in Figure 1 (see page 137). The majority (63%) of the firms included all their products in the 1978 ABPI data sheet compendium and a further 10% included all but two of the products.

Whether or not all the products were included, those mentioned were considered (for the purpose of this study) to represent the full product range for which the information department was responsible. Since some firms market several different products which belong to the same pharmacological

TABLE 4

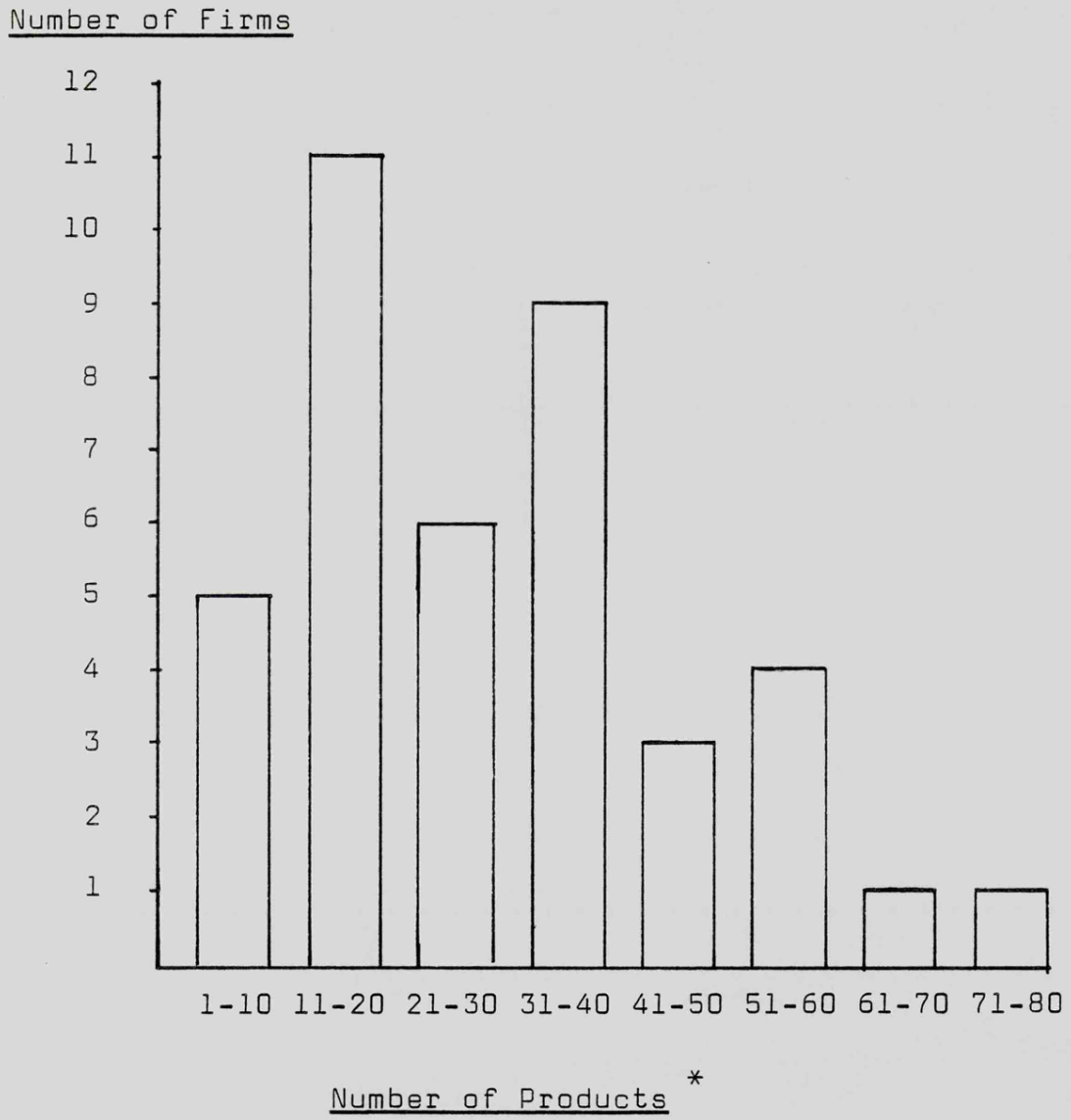
ADDITIONAL DUTIES CARRIED OUT BY INFORMATION STAFF

Duty	Information Department carrying out the duty	
	No.	%
Organising and running clinical and/or post marketing trials	9	23
Writing technical booklets	9	23
Product registration and/ or preparation of CSM* submissions	6	15
Checking advertising copy	12	30
Checking technical booklets	4	10
Adverse drug reaction monitoring	3	8
Others - miscellaneous	3	8

*Committee on Safety of Medicines

FIGURE 1

THE NUMBER OF PRODUCTS MARKETED BY THE FIRMS STUDIED



* The number of products refers to the number included in the 1978 ABPI Data Sheet Compendium.

category (e.g. antidepressants, oral contraceptives), the number of categories that each product range covered was determined. The pharmacological categories used were listed in the April 1978 issue of the Monthly Index of Medical Specialities (MIMS). (The category to which any particular product belonged was determined either from the index listed in MIMS or from the stated uses or indications in the data sheet compendium. If no category was appropriate, e.g. for X-ray contrast media, additional ones were created.) The average number of products each firm had in each category was 1.8 (ranging from 0.8 to 4.1). The distribution of pharmacological categories is shown in Figure 2 (see page 139).

As would be expected, more information staff were employed both in firms marketing more products ($P<0.05$) and in firms having products in more pharmacological categories ($P<0.01$).

4. Information Resources used by Information Departments

Three questions were asked to find out which resources were available to information departments (or their equivalent), in the firms visited. The first question dealt with access or subscriptions to information systems, and the results are shown in Table 5 (see page 140).

The number of resources available to each firm mainly reflects the size of the budget for information work (which is partly dependent on the profitability of the firm). For this reason, no direct comparison of the resources of different firms was made. However, the number of firms having access to one or more resources providing either references lists of recent publications or abstracts of recent articles is shown

FIGURE 2

THE NUMBER OF THERAPEUTIC CATEGORIES COVERED BY THE PRODUCT RANGES OF THE FIRMS STUDIED

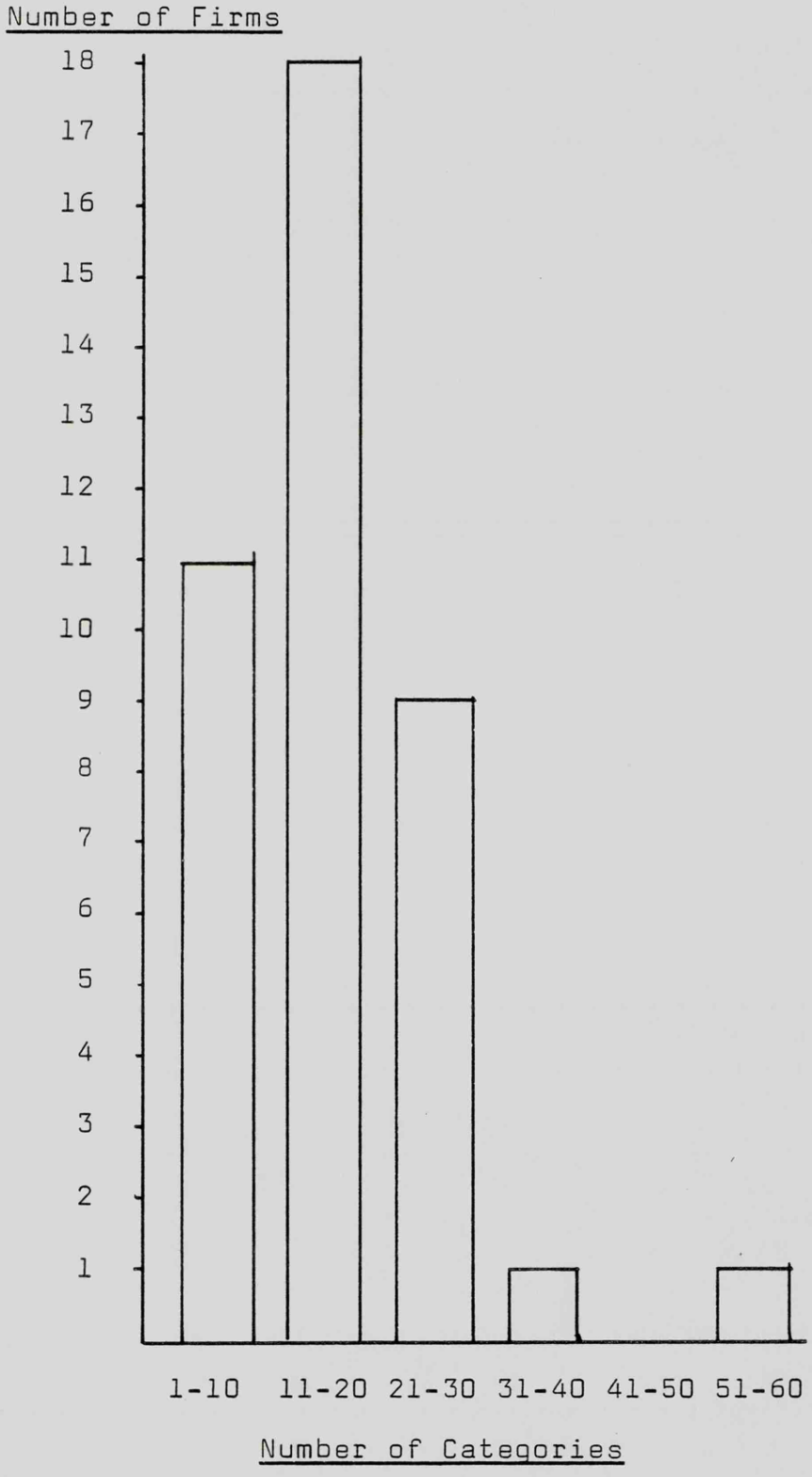


TABLE 5

RESOURCES AVAILABLE TO INFORMATION STAFF

Information System	Firms having access to the system No.	%
Providing Reference Lists		
Index Medicus	28	70
Current Contents/Clinical Practice	28	70
MEDLINE	20	50
BLAISE	9	23
MEDLARS	9	23
ASCA	8	20
Science Citation Index	3	8
Providing Abstracts		
RINGDOC	16	40
TOXLINE	11	28
Excerpta Medica	11	28
International Pharmaceutical Abstracts	7	18
BIOSIS	4	10
DRUGDOC	2	5
Biological Abstracts	2	5
de Haen Services	2	5
Other abstracting publications	5	13
Miscellaneous		
Parent Company outside the U.K.	25	81*
Unlisted Drugs	8	20
Index of New Products	6	15
FARMDOC	3	8

* denotes percentage of non-U.K. companies.

in Table 6. (Nintyfive percent of the firms visited have access to at least one information source.)

TABLE 6

ACCESS TO INFORMATION RESOURCES

Firms having access to at least one information resource	Firms Number	%
Providing Reference Lists	34	85
Providing Abstracts	26	65
Parent Company	25	81*
Other Miscellaneous resources (excluding Parent Company)	12	30
Firms not having access to any of the above resources	2	5

* expressed as a percentage of non-U.K. based companies.

The second question dealing with information gathering asked which medical journals were taken either by the department or the company as a whole. Sixtythree percent of the firms provided journal holdings lists for the company, and a further eight percent provided either the information department's own list of journals holdings, or the list of journals circulated to information staff.

No direct comparison of the total number of journals held by each company was made, because this would largely

be determined by the type of products marketed and funds available. However, the range of different subjects covered by the medical journals holdings was estimated. The subject categories were based on the medical specialities listed in the Health and Personal Social Service Statistics for England (1976), excluding those that did not use drug therapy. The subject categories are shown in Appendix 5C. The journals held by each of the 28 companies were placed in the most appropriate category and the subject coverage for these companies is shown in Table 7.

TABLE 7

NUMBER OF SUBJECTS COVERED BY JOURNAL HOLDINGS

Number of subjects	Company Lists Provided Number	%	Department Lists Provided Number	%
1 - 5	4	10		
6 - 10	4	10	1	3
11 - 15	10	25		
16 - 20	3	7	1	3
21 - 25	1	3	1	3
26 - 30	2	5		
more than 30	1	3		
Total	25	63	3	9
mean number of subjects covered	13.8		17.7	

The average number of subjects covered by the 25 firms providing company library lists was between 11 and 15 subjects (the modal class). Twelve firms did not provide either company or department journal holdings lists and therefore there was no estimation of subject coverage by these firms.

The third question asked the respondent to state any additional information resources that were used, excluding information systems, journals and unpublished company reports. The results are shown in Table 8.

TABLE 8

ADDITIONAL INFORMATION SOURCES USED BY INFORMATION STAFF

Source	Firms using Source No.	%
Formal		
Textbooks	9	23
Libraries	8	20
ABPI	2	5
Informal		
Contacts with doctors	7	18
Pharmacy training	2	5
Recognised authorities	2	5
Contacts in other drug firms	2	5
Contacts with pharmacists	2	5
Formal/Informal		
Parent Company (not U.K.firms)	25	81*
Symposia	6	15
Own non-U.K. subsidiaries (U.K. firms)	4	44+

* expressed as % of non U.K. firms + expressed as% of U.K. firms

The data were not necessarily complete but probably include resources used regularly by the information staff.

5. Factors affecting information provision to the medical profession

All 40 companies used reprints or photocopies of published articles to answer enquiries from the medical profession. Provision of other information is shown in Table 9.

TABLE 9

PROVISION OF INFORMATION TO ANSWER ENQUIRIES FROM THE MEDICAL PROFESSION

Information	Firms using information					
	Regularly		Occasionally		Abstract or quote from	
	No.	%	No.	%	No.	%
Reprints/photocopies of journal articles	40	100	-	-	-	-
Technical booklets	35	88	1	3	-	-
Sales promotion literature	20	50	12	30	-	-
Unpublished company reports	17	43	8	20	12	30
Other educational information	16	40	-	-	-	-

Technical booklets were defined as product guides designed to provide prescribing information. A details analysis of the information content of the 36 technical booklets provided by the firms visited is described in Appendix 5D.

Only two firms provided two technical booklets for the same product, each containing different levels of information. In both cases, one was designed for use by general practitioners and the other for use by hospital doctors.

Educational information included symposia proceedings, drug interaction charts and disease orientated manuals.

The respondents were asked what information was sent to a member of the medical profession who requested full prescribing information about a particular product. The results are shown in Table 10.

TABLE 10

INFORMATION PROVIDED IN RESPONSE TO A REQUEST FOR FULL PRESCRIBING INFORMATION

Information Provided	Firms No.	Firms %
A relevant data sheet only	5	13
A relevant data sheet plus a technical booklet	27	68
Selection of major articles as reprints or photocopies	12	30
List of references	4	10
Selection of promotional material	2	5
Enquiries processed by sales promotion departments	4	10

A data sheet is a legal document which provides the

practitioner with an objective statement (in a convenient form for reference), giving essential particulars about the medicinal product. (The exact requirements for a data sheet are discussed in Chapter 1.)

The pharmaceutical industry is obliged to provide a data sheet to all medically qualified enquirers requesting full prescribing information. Seventyeight percent of the respondents stated that they provided other information in addition to this legal minimum. (This total excludes the firms in which the sales promotion departments answer an enquiry asking for full prescribing information.)

Respondents in the five firms that only provided a data sheet were asked whether their company considered that the data sheet provided full prescribing information. All five stated that it did do so.

Fifty percent of the respondents indicated that the material sent to an enquirer asking for full prescribing information depended on his status. Table 11 (see page 147) shows the factors affecting the material provided.

The information included with a response to a specific question is shown in Table 12 (see page 148).

Fourtyfive percent of the firms included some general information in an answer to a specific question. (This total excluded the respondents who stated that provision of general information with the specific answer would depend on the actual question that was asked.)

Reprints (not photocopies) of published articles were distributed by all 40 firms in response to relevant enquiries. The factors which determined which reprints were kept for this purpose are shown in Table 13 (see page 149).

TABLE 11

FACTORS AFFECTING THE MATERIAL PROVIDED IN RESPONSE TO A REQUEST FOR FULL PRESCRIBING INFORMATION

Factors	Firms No.	Firms %	Effect	No. of Firms
Hospital doctors or G.P.s	17	43	Hospital doctors are provided with more information	16
			Difference not specified	1
Para-medical staff and medical doctors	2	5	Difference not specified	2
Products themselves	1	3	Difference not specified	1

TABLE 12

INFORMATION PROVIDED IN RESPONSE TO A SPECIFIC QUESTION

Information Provided	Firms No.	Firms %
Appropriate specific answer only	15	38
Appropriate specific answer plus		
a relevant data sheet	11	28
a technical booklet	8	20
Reprints or photocopies of journal articles	2	5
Promotional material	1	3
Inclusion of other information would depend on the question asked	7	18

TABLE 13

FACTORS AFFECTING WHICH REPRINTS ARE KEPT FOR DISTRIBUTION IN RESPONSE TO RELEVANT ENQUIRIES

Factors	No. of Firms	% of the total firms mentioning each factor *	% of total factors
Papers showing own products in a favourable light	16	40	27
Assessment of the usefulness of the paper to answer common questions	15	38	25
Well conducted, valid clinical trial reports	5	13	9
Country of origin of the paper (U.K. and U.S. papers preferred)	3	8	5
Balance of good papers showing own products in positive and negative lights	2	5	3
Date of publication - most recent papers preferred	1	3	2
Those containing the most information	1	3	2
Cost of reprints	1	3	2
Place of publication - high circulation journals preferred	1	3	2
Recognition of the trialists in terms of standing in the medical community	1	3	2
Not aware of any specific factors	13	33	22

* This column totals more than 100% because some firms mentioned more than one factor

Finally, in assessment of information provision, three hypothetical questions concerning adverse reactions, drug interactions and comparison with competitors' products were asked. The aim of these questions was to discover which sources of information would be used for the reply.

In response to "do you know of any adverse reactions likely to occur with the administration of your product +++++?", all 40 information departments would search their own national or international files containing published and unpublished data. Twentyfive firms stated that in addition, the resources shown in Table 14 would be checked.

TABLE 14

RESOURCES USED FOR PROVIDING INFORMATION ON POSSIBLE ADVERSE REACTIONS

Resources	Firms No.	Firms %
Own national/international data file containing published and unpublished information only	15	38
Own data file plus		
CSM bulletins	23	58
Textbooks	10	25
On-line computer retrieval facilities	3	7

The resources used to answer a question concerning drug interactions likely to occur with the administration of a particular product are shown in Table 15. Again all the firms would search their own national or international file of published and unpublished data.

TABLE 15

RESOURCES USED TO PROVIDE INFORMATION ON POSSIBLE DRUG INTERACTIONS

Resources	Firms No.	Firms %
Own national/international data file containing published and unpublished information only	15	38
Own data file plus		
CSM bulletins	9	23
Textbooks	19	48
On-line computer facilities	3	8
Offer of theoretical predictions	4	10
Stockley's interaction data *	4	10

* Stockley I, Drug Interactions and their Mechanisms, London, Pharmaceutical Press, 1974.

The information that would be provided in response to a question concerning a comparison of their own and a competitor's product is shown in Table 16. Ninetyeight percent of the firms stated that they would provide published comparative clinical trial reports (see page 152).

TABLE 16

INFORMATION PROVIDED FOR COMPARISON OF EFFICACY OF OWN AND COMPETITORS' PRODUCTS

Information Provided	Firms No.	Firms %
Published comparative clinical trial reports	39	98
Published reports plus		
Technical booklet of own product	5	13
Unpublished clinical trial data if a comparison between own products is requested	1	3
Comments on the conduct, results and validity of the trials	1	3
Procedure if no direct comparison exists		
Suggest enquirer carries out a trial	5	13
Provide review articles of the subject area	4	10
Suggest pharmacodynamic aspects to enable a comparison	2	5
Procedure if enquiry concerns an ongoing trial		
The enquirer is allowed to contact the trialist	1	3
Enquiries of this nature are dealt with by clinical trial departments	1	3

The majority of firms do not provide any information if no published comparative clinical trial report exists. This was because the information staff felt that they did not possess sufficient information on competitors' products to permit them to evaluate objectively the relative efficacy of their own and competitors products.

6. Availability, efficiency and use of information departments

It was possible to contact the majority (93%) of information departments between 09:00 and 17:00 on weekdays. Thirtyfive percent were available before 09:00 and 53% after 17:00.

Eighty percent of all firms have some form of 24 hour emergency cover, usually the night security staff provided the home telephone number of medical directors or information staff. The type of emergency cover is shown in Table 17 (see page 154).

Firms not providing any emergency cover employ significantly fewer information staff than those providing cover, ($P<0.01$). The provision of the 24 hour emergency cover did not depend on the number of products marketed by each company.

The efficiency of provision of information was assessed by the average length of time taken to reply to a written enquiry or a telephoned request that could not be answered immediately. It was necessary to consider the average time to reply, because the responses to some written requests would be known immediately without reference to any resources, whereas

TABLE 17

AVAILABILITY AND TYPE OF EMERGENCY COVER PROVIDED BY THE FIRMS VISITED

Type of cover	Firms No.	Firms %
None	12	30
Night security staff provide telephone numbers for medical and/or information staff	17	43
"Ansafone" service, recorded message provides telephone numbers of medical and/or information staff	8	20
D.H.S.S. have home phone numbers of key medical personnel in firm	2	5
Cover exists but was not described*	1	3

* This result was recorded on one of the two questionnaires returned.

at the other extreme, delays could occur due to off-line print outs from on-line computer retrieval systems taking several days to arrive.

The responses may represent a range from a rarely achieved ideal, to actual behaviour. The results are shown in Table 18.

TABLE 18

TIME TAKEN TO REPLY TO REQUESTS

Requests	Firms No.	Firms %
Written		
Reply provided within 24 hours	16	40
" " " 2 days	7	18
" " " 3 days	4	10
" " " 4 days	1	3
" " " 5 days	11	28
" " " 2 weeks	1	3
Telephoned requests		
Reply provided within 24 hours	33	83
" " " 2 days	5	13
" " " 3 days	1	3
" " " 5 days	1	2

If the reply given fell into more than one category, either the mean length of time, or, in the case of two adjacent categories, the slower reply time, was recorded.

Replies to telephoned requests were provided significantly faster than replies to written requests ($P<0.001$). In both cases, the majority of replies were provided within three days of receipt.

Interestingly, neither the number of information staff employed by the firm, nor the number of products for which the department was responsible, affected the length of time taken to provide a reply.

All respondents were asked to state approximately how many enquiries their department received in the week preceding the interview, by telephone, in the post and from representatives on behalf of recently visited doctors. Several firms kept complete records and were able to provide exact data, but the majority were only able to estimate the number of enquiries received. Four of the firms had very recently launched new products and the numbers of enquiries received were considerably higher than usual. The results are shown in Tables 19 and 20(see pages 157 and 158).

Eight respondents were unable to estimate the total number of enquiries received ineither the preceding week or a typical week. Three others did not record the type of enquiry (written or telephoned) but did know the total number received. Eighteen were unable to state the number of enquiries received via representatives (on behalf of recently visited doctors). This was because these enquiries tended to be collected by sales promotion departments and passed on to the information department in batches.

Most firms received twice as many telephoned requests as enquiries by post or via representatives. As many of the

TABLE 19

NUMBER OF ENQUIRIES RECEIVED IN THE WEEK PRECEDING THE INVERVIEW

Total No. of Enquiries	Firms No.	%
1 - 20	1	3
21 - 40	6	15
41 - 60	8	20
61 - 80	8	20
81 - 100	4	10
101- 150	3	8
more than 150	2	5
Do not know	8	20

TABLE 20

ROUTE OF ENQUIRIES RECEIVED IN THE WEEK PRECEDING THE INTERVIEW

No. of Enquiries	Telephoned Firms No.	%	In the Post Firms No.	%	Via Representatives Firms No.	%
1 - 10	4	10	12	30	9	23
11 - 20	7	18	8	20	6	15
21 - 30	4	10	3	8	5	13
31 - 40	6	15	3	8	-	-
41 - 50	3	8	1	3	1	3
51 - 60	4	10	2	5	-	-
61 - 70	-	-	-	-	-	-
71 - 80	-	-	-	-	-	-
81 - 90	1	3	-	-	-	-
none	-	-	-	-	1	3
do not know	11	28	11	28	18	45

replies were only estimated totals, and four companies had specifically stated that the totals for the previous week were higher than average, the data were presented in fairly broad categories. In addition, a question of this nature might well be prone to exaggeration, particularly if answering enquiries justified the existence of the information department.

As would be expected, the more products for which the department was responsible, the more enquiries it received ($P<0.05$). However, the total number of enquiries received did not affect either the number of information staff employed by the firm, or the length of time taken to reply to either a telephoned or written request. This is explained diagramatically in Figure 3 (see page 160).

Nineteen respondents (48%) reported that some doctors wrote regularly for information about drugs. The reasons for doing so, suggested by the respondents, are shown in Table 21.

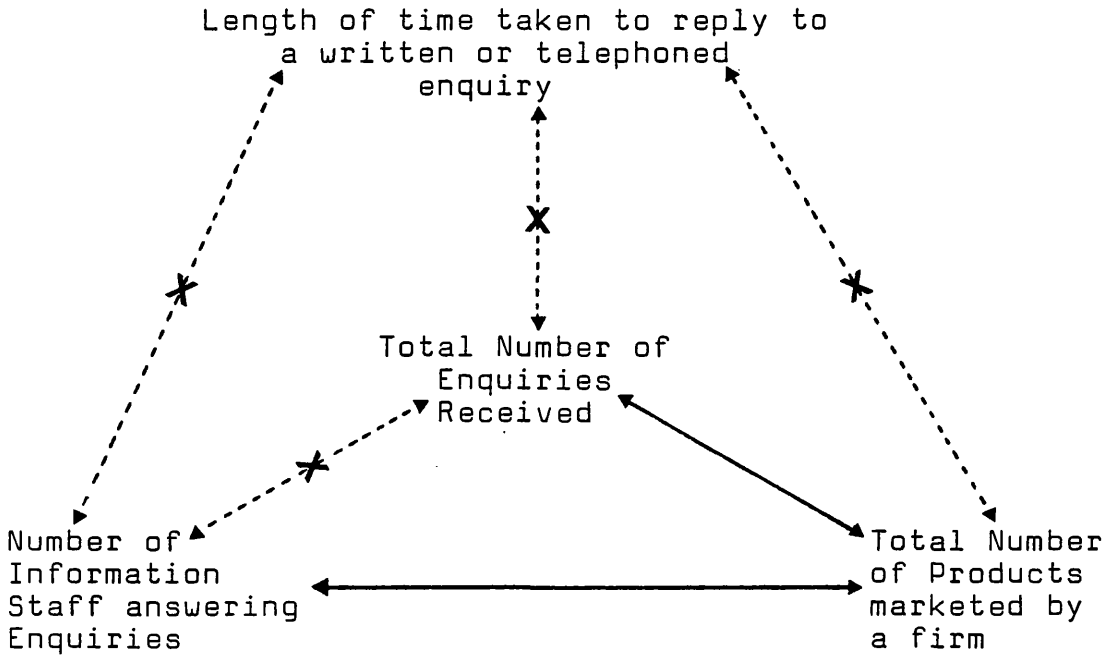
TABLE 21

REASONS FOR WRITING REGULARLY FOR INFORMATION

Reason	Firms No.	Firms %
To use the information department as an updating service	13	33
To use a service that has been helpful on previous occasions	7	18
To ask relatively obscure questions about particular products	4	10
To obtain research information (clinical investigators only)	3	8

FIGURE 3

FACTORS AFFECTING THE LENGTH OF TIME TAKEN TO REPLY TO AN ENQUIRY



denotes a directly proportional relationship

denotes no relationship

7. Type of Enquiries Received by the Information Departments

The respondents were asked to state what type of information request was received most often. To obtain accurate data, each member of the information department would be required to monitor all enquiries received over a long period of time. This was considered an unreasonable request. Therefore, the responses to this question represented the opinion of the member of the department who was interviewed. As the majority of the respondents mentioned more than one type of request, the most common ones are probably included. The results are shown in Table 22 (see page 162).

Eight of the respondents were unable to answer the question because they felt that either too many information requests were common or that the type of enquiry depended mainly on the current promotional campaign. Four other respondents, who did state which enquiries were the most common, pointed out that the requests tended to depend on current themes in the medical press, or seasonal ailments such as hayfever, coughs and colds etc. Fourtyfour percent of the enquiries concerned clinical information, and a further 23% required essential prescribing details. Thus the majority of enquiries concerned use of a product in a clinical situation.

Twentynine respondents received enquiries for products that could be bought by the general public without a prescription (non-prescription drugs). In all but one case, this type of enquiry differed from those received concerning prescription products. The differences are shown in Table 23 (see page 163).

TABLE 22

THE MOST COMMON INFORMATION REQUESTS RECEIVED BY INFORMATION DEPARTMENTS

Requests	Firms No.	Firms %	% of total Requests
Basic Prescribing Information			
Full prescribing information	10	25	13
Dosage and administration	8	20	10
Practical Clinical Information			
Interactions with other drugs	9	23	11
Side effects	9	23	11
Safety in pregnancy	7	18	9
Compatability with other products e.g. in infusion fluids	4	10	5
Excretion in breast milk	3	8	4
Adverse drug reactions	2	5	3
Action to be taken in the case of poisoning	1	3	1
Practical Pharmaceutical Information			
Pharmaceutical precautions	9	23	11
Theoretical Information			
Pharmacology and metabolism of drugs	5	13	6
Use of products in unauthorised indications	3	8	4
Clinical evidence for the claims made	3	8	4
Use of products in minority patient groups e.g. paediatric, geriatric	2	5	3
Enquiries about diseases	1	3	1
Miscellaneous			
Enquiries concerning specific products	3	8	4
Full information (for drug information centres)	1	3	1

TABLE 23

DIFFERENCE IN THE TYPE OF ENQUIRY CONCERNING PRESCRIPTION AND NON PRESCRIPTION DRUGS

Difference	Firms No.	Firms %*
Type of Enquiry Differs		
Enquiries for non-prescription medicines are usually more precise	2	5
Enquirer Differs		
Enquiries for non-prescription medicines are more likely to originate from		
the public	22	55
retail pharmacists	8	20
other para-medical staff	3	8
newly qualified doctors	1	3
no difference	1	3

* Several of the 29 respondents mentioned more than one difference.

8. Relationship with and Opinions of Hospital Drug Information Centres

Only 11 (28%) of the firms participating in this study liaised with any hospital drug information centre, although all 40 answered specific enquiries received from these centres. The liaison usually took the form of information bulletins, as shown in Table 24.

TABLE 24

LIAISON WITH HOSPITAL DRUG INFORMATION CENTRES

Type of Liaison	Firms No.	Firms %
Send all general mailings	4	10
Provide regular information bulletins	2	5
Visit to ensure that they are kept up-to-date	2	5
Provide with bulletins if a particular enquiry becomes common	1	3

The respondents were asked about their opinion of hospital drug information centres. The results are shown in Table 25 (see page 165). Opinions were classified as positive, negative or non-committal. Eighteen percent of the respondents viewed the centres in a positive light; 43% in a negative light; 13% were non-committal; and the remaining 28% stated a mixture of positive, negative and non-committal views.

TABLE 25

OPINIONS OF HOSPITAL DRUG INFORMATION CENTRES

Opinions	Firms No.	Firms %	% of total Opinions
Positive Views			
Drug Information Centres (DIC) are useful focal points for receiving information from the industry	6	15	8
DIC are easily accessible for medical staff in hospitals	4	10	6
DIC have a useful function (unspecified)	3	8	4
DIC are useful mediators of enquiries from the medical profession	2	5	3
			21%
Negative Views			
DIC are poor mediators of enquiries from the medical profession	14	35	20
DIC do not have the resources to provide the same depth of information as industry based information departments	14	35	20
DIC staff are too inexperienced for the responsibility that the position demands	5	13	7
DIC are attempting to duplicate the resources of the industry	4	10	6
DIC are not used by G.P.s	3	8	4
DIC staff tend to rely on their own possibly inadequate information rather than check with the relevant company	2	5	3
DIC staff tend to consider themselves unbiased, which is probably untrue because they have limited drug information	2	5	3
DIC staff are evaluating product efficacy and advising medical staff on this basis	2	5	3
DIC staff claim to provide more scientific information than industry based information departments	1	3	1
			66%
Non-Committal Views			
DIC function is not defined	4	10	6
No experience of them	3	8	4
It is impossible to generalise about the value of DIC as some are good, some bad	2	5	3
			13%

9. Opinions of Bias in the Provision of Information by Information Staff in the Industry

Seventythree percent of the respondents stated that, in their opinion, medical information departments provided unbiased information on their own company's products. Twentytwo of these respondents referred to their own information department to answer this question. Eight of the 11 respondents who felt that biased information was provided, also referred to their own company. Table 26 shows the range of comments made by the respondents when asked to state why they felt that either biased or unbiased information was provided (see page 167).

DISCUSSION

1. Problems of Interview Design

As the pharmaceutical industry is highly competitive and some firms have considerably larger funds available for information work, the competitive element could affect responses to even the most straight-forward questions. In an attempt to avoid this, the confidentiality of the data provided by the respondents was guaranteed. However, this would not necessarily prevent exaggeration of information resources and describing ideal behaviour for the department or its equivalent.

Questions relating to how the information department obtained its information were particularly prone to problems. This was because it was obvious after a few interviews that the definition of information system varied from person to person (see question 5, Appendix A). To some respondents, it meant only information data bases, using computer retrieval facilities, whereas other respondents also included conventionally

TABLE 26

COMMENTS MADE ABOUT THE PROVISION OF BIASED OR UNBIASED INFORMATION

Comments	Firms No.	Firms %	% of total Comments
Unbiased Information			
"The department's function is to be unbiased"	17	43	41
"Professional ethics prevent us from providing biased information"	5	13	12
"We answer enquiries as truthfully as our knowledge permits"	4	10	10
"We provide a fair balance of information"	4	10	10
"We provide factual and complete information"	4	10	10
"To ensure that we are used on future occasions, we always provide unbiased information"	2	5	5
"We would never supress side effects"	2	5	5
"We would even recommend a competitor's product if it was relevant to do so"	2	5	5
"We only provide papers, not opinion"	2	5	5
			100
Biased Information			
"We tend to select papers that show our products in a good light"	8	20	67
"It is impossible to provide unbiased information"	4	10	33
			100

published resources. It was decided that a prompt list might encourage exaggeration of resources, and that sources commonly used would probably be mentioned. Fortunately, 63% of the firms provided a list of the journal holdings of the company library, and this was used to check that all conventional publications had been included. The intended meaning of information system was made clear to respondents in the remaining companies.

Other complications concerning access to information occurred because the majority of companies visited were subsidiaries of multi-national companies, with parent companies based outside Britain. The U.K. subsidiaries had access to the information resources purchased by their parent company (usually by sending a telex request for information) but the staff in the U.K. subsidiaries were not always aware exactly which sources were available. For this reason, the results may not include every resource available to each firm.

The hypothetical questions that were asked to assess use of the available information resources were general questions, as it was impossible to design specific questions of equal complexity for each firm visited. The disadvantage (as several respondents pointed out) was that general questions concerning adverse reactions and drug interactions were very rarely asked.

The question concerning the effect of bias on the information provided was designed to assess the respondents' concept of bias. It is very difficult to assess bias objectively, but the majority of the respondents welcomed

the opportunity to discuss its effect on provision of information.

2. Nationality of the Parent Company

Companies based in Britain have easy accessible information resources, whereas those based outside the U.K. usually have access to resources used by their parent company. They therefore tend to have fewer resources on hand. This factor may give the nine British owned companies an advantage in situations when the required information is available only from a parent company, which collates information for all its subsidiaries.

3. General Characteristics of the Information Department

The 88% of firms that had a specific medical information department may be more easily able to separate the information function of the firm from the commercial pressures of the other departments. This separation may also prevent conflicts of conscience occurring for the information staff.

Qualifications held by the staff answering enquiries were considered important because information staff need to provide evaluated information.[2] The industry appears to agree with this view, as 90% of the staff held some formal or para-medical qualification.

4. Resources used by Information Departments

Direct comparison of resources available to the companies visited would probably only reflect the size of the information budget. The value of any particular resource to a company will depend on:

1. the number of products, and type of product range;
2. the total number of resources available;
3. the number of competitive products on the market;
4. characteristics of the resource, e.g. how quickly after publication the information appears in the resource.

Ashmole et al[3] studied the cost-effectiveness of current-awareness sources in the pharmaceutical industry and came to the conclusion that for a specific product, no single source could be relied upon to give adequate coverage. Some resources were more effective than others.

For information staff to be aware of all published articles concerning their products, they need to have access to several resources, or to visit major medical libraries regularly. Not all information departments achieve this ideal, particularly in companies with small product ranges. Regular visits to major medical libraries would also supplement journal and textbook holdings.

5. Information Provision

Any information provided by the pharmaceutical industry could probably be considered promotional, including reprints (or photocopies) of published articles, which may be provided to enhance either product or company image. If an enquirer has solicited information and the information provided is factual, accurate and relevant to the original request, the promotional aspect is probably not important to the recipient.

The ability of sales promotion literature to answer a particular enquiry would depend on the enquiry and the information content of the literature. However, if the

advertising message tends to overshadow the information required by the enquirer, it might be preferable to use other material, rather than provide obviously biased information.

Information provided in response to a request for full prescribing information varied from the relevant data sheet alone, to relevant reprints of published articles and a technical booklet (in addition to a data sheet). The data sheet does not provide all the important prescribing information required by hospital doctors (see Chapter 2). The majority of technical booklets also do not include this information (see Appendix 5D). It is doubtful that reprints of published articles would do so. To ensure that the prescribing doctor receives the information that he requires in a concise format it might be worthwhile improving the data sheet rather than standardising technical booklets. It appears that some technical booklets are informative sales promotion literature.

The 17 respondents who stated that more detailed full prescribing information was provided to hospital doctors than to general practitioners, did not offer to explain why this was done. It is possible that the distinction is made because general practitioners have little time available to read detailed information, but since information has been specifically requested, this distinction may be unnecessary. The rationale behind providing hospital doctors with copies of published articles and general practitioners with a list of references could be questioned, because hospital doctors usually have easier access to medical libraries than general practitioners.

Inclusion of general information with a reply to a specific question obviously depends on the question asked and whether the respondent feels that the question asked is the question intended. However, in general, 38% of the firms do not provide general information, whilst 45% do provide some. If more information is being provided than is necessary, this may be done to disguise inability to answer a question or to use the opportunity to promote either the product or the company image.

Reprints of published articles kept to answer relevant enquiries have been selected for this purpose, because it is impossible to obtain reprints of all papers mentioning any particular product. If the 16 firms that select papers showing their own products in a favourable light, also fail to mention other published papers which may be relevant, they are obviously providing biased information. A statement about any other published evidence, or lack of it, may be a valuable addition to any replies containing reprints.

The resources used for providing information on possible adverse reactions and drug interactions depends on resources available. Published reports of this kind can appear in a wide range of publications, highlighting the necessity to have access to several current-awareness information systems. Unpublished information on both these topics can be extensive, and most firms follow up in detail any incidents reported to them. Bulletins issued by the Committee on Safety of Medicines (CSM) are the source used by the majority of firms to check on adverse reactions, in addition to their own file of published and unpublished data.

The bulletins from the CSM are of limited value, because they only list the incidence of adverse reactions to any product. It is impossible to check whether the reaction stated occurred as a result of administration of the product indicated in the report. Currently there is much debate about the problems associated with the collection and dissemination of this information by regulatory bodies, the industry and the medical profession. The current status and proposed solutions are discussed in Appendix 5E.

Textbooks are the most frequently used source of information about drug interactions, in addition to each company's own files of published and unpublished data. Although many textbooks are available, due to the time taken for publication, textbooks cannot be considered an ideal up-to-date source.

Information provided in response to an enquiry concerning a comparison with a competitor's product would always take the form of a published comparative clinical trial report, if one was available. No company would offer information on a competitor's product, unless it was published and, hence, the industry is not a good source for comparing product efficacy.

6. Availability, Efficacy and Use of Information Departments

It was noted that some smaller firms did not consider that they had a responsibility to provide information concerning emergencies outside the working day. It was not clear whether these firms marketed "safer" products (e.g. less likely to be hazardous in overdosage etc.) or whether the inconvenience caused to the small number of information staff in these firms affected this decision.

Some firms appear to be more efficient in responding to enquiries and, therefore, perhaps the service in some could improve. Lack of secretarial assistance was blamed in some cases, although, if necessary, the telephone could be used to reply to written requests.

As the efficiency of the service did not depend on the number of staff employed, nor the number of products marketed by the firm, provision of drug information to the medical profession may not be the primary function of the information department in many firms.

The majority of firms received more than 40 enquiries from the medical profession each week. This is approximately double the average number of enquiries received by eight NHS regional drug information centres in 1974,[4] even though these centres provide information on a much larger product range than any medical information department in the industry. This suggests that the service provided by the industry is not being replaced by the service provided by drug information centres (see also Appendix 5F).

Nineteen firms reported that some doctors wrote regularly for information, the majority for information to keep them up-to-date. This implies that the information provided on previous occasions was useful and trustworthy.

7. Type of Enquiry

The majority of enquiries received by industry departments were practical questions concerning the use of drugs in clinical situations. NHS drug information centres appear to obtain a similar range of enquiries, although they tended to receive more queries about adverse reactions.[4]

Industry medical information departments seemed more likely to receive enquiries concerning drug interactions, but were less likely to be asked for pharmaceutical information than their NHS counterparts.

Approximately half the firms received enquiries about products that could be bought without a prescription, usually from the public or retail chemists. However, most respondents stated that these enquiries were rare.

8. Relationship with and Opinions of Hospital Drug Information Centres

Of the 11 firms that actively liaised with drug information centres, only four expressed any positive views about the centres. A further four realised that drug information centres did not have the resources, time, staff and space etc. to accumulate the same depth of knowledge as industry information departments and attempted to make their task easier, by providing information to them.

It is interesting to note that 20% of the centres found that drug information centres were poor mediators of enquiries originating from medical staff. Rogers and Barrett in a paper discussing the establishment of the drug information centre at the London Hospital stated

> "We have found that it is best to speak directly to the questioner (rather than rely on a message passed via a third person) in order to avoid answering the wrong question."[5]

This suggests that at least some information pharmacists are aware of this problem and could attempt to avoid criticisms of this nature.

Although NHS based drug information centres do not have the

same financial resources as industry information departments, the actual relevance of these resources to the provision of information is questionable, particularly if liaison between industry and the NHS centres is improved. Very detailed information is not generally necessary for the provision of basic prescribing details.

The concern that staff in NHS based centres are "too inexperienced" was a personal view expressed by five respondents. It may simply reflect the type of enquiry that they have received. No information is available describing the type of qualifications and experience of information pharmacists, in NHS based centres.

Four respondents commented that they had received requests for "full information" on all their products from drug information centres. All four complained that to do this would require a considerable amount of time and effort, and felt that information pharmacists should contact the relevant pharmaceutical firm with specific enquiries when they were received. This would save the industry from providing information that might never be used, and drug information centres from storing unnecessary data.

The fear that drug information centres are not used by general practitioners, who prescribe the majority of drugs used by NHS patients, is well founded. Leach[4] and McCabe et al[6] both reported very low use of eight British and one Scottish regional drug information centre respectively, by general practitioners. The reason for this has not been studied.

Two respondents felt that drug information centres tended to rely on their own, possibly inadequate, information

rather than contact drug firms with specific queries. Neither respondent was able to provide any evidence to support this belief.

Similarly, no evidence was provided for the views that NHS drug information centres consider themselves unbiased (although this is implied by Blacow[7]), nor that drug information centres are assessing product efficacy and advising medical staff of "best buys" on this basis. Closer liaison with industry information departments could remove these fears.

Katz and Triboletti[8] suggested that the pharmaceutical industry has an obligation to provide clinical pharmacists with comprehensive information on all marketed products. They proposed a standard format which would allow the clinical pharmacist to have all the knowledge that he requires in one convenient source. This would require considerable time and effort to prepare and constant revision to keep up-to-date. It would also duplicate a large amount of information (which is wasteful) and probably cause resentment in the industry, as the arrangement would only benefit drug information centres. Their present lack of use in the U.K. does not seem to justify this suggestion.[4,6]

The literature comparing the British and American experience of drug information centres is reviewed in Appendix 5F.

One possible suggestion to avoid the total duplication of the information accumulated by the industry in each drug information centre, would be to allow the centres to have access to industry's vast information resources and information.

In return, the centres could provide detailed information

on products in clinical use (particularly in minority patient groups that are excluded from clinical trials e.g. use of a product in pregnancy).

9. Bias in Industry Medical Information Departments

The problems concerning definition of bias have already been noted and are particularly highlighted by comments such as "we only provide papers and not opinion". The majority of the respondents who claimed that either information staff in their own firm, or in pharmaceutical industry in general, provided unbiased information, appeared to separate the information function from all other activities of the industry. Despite good intentions, the employment of these staff does depend on the firm's commercial success and therefore the provision of biased information may be justified unconsciously.

On the other hand,the industry cannot afford to provide deliberately misleading information because it is against their code of practice (see Appendix 5G). It could also cause serious damage to the image of the company.

Those firms recognising bias in the information provided did not cite serious examples of bias.

Several respondents felt that the industry as a whole could take a positive stand on the provision of biased information because those firms providing a valuable information service could be adversely affected by those firms having lower standards. One possible area for improvement would be to ensure that references to published information are not omitted from a reply because the articles do not recommend the use of the firm's products.

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APPENDIX 5A

INFORMATION PROVIDED BY THE PHARMACEUTICAL INDUSTRY

Company _____

1. Does your company have a drug information department which deals with enquiries from the medical profession ?

YES ☐ NO ☐

If NO, please state which department deals with enquiries from the medical profession

_____

2. How many staff does this department employ ? ☐

3. What academic qualifications are held by the staff who answer enquiries from the medical profession ?

	No.		No.
MB BS	☐	B.Sc	☐
PhD	☐	M.Sc	☐
MPS	☐		

Others - please state and add number

_____

4. How many products does your firm have on the market at the moment ? (products = number of preparations that have different indications)

Prescription only medicines	☐
Prescribable over the counter drugs	☐
Non prescribable over the counter drugs	☐

5. Does your department subscribe to, or have access to, any information systems (computer based or traditional publications) ?

YES ☐ NO ☐

If YES, please state which sources

_____

6. Please list below all the journals to which you subscribe either as a department or as a company

   OR please may I have a copy of your journals holdings list ?

7. Do you obtain information from any other sources apart from the following ?

   Journals

   Unpublished company reports

   Information systems such as those mentioned in question 5

   YES ☐ NO ☐

   If YES, please state which sources

   _____

8. Does your department (or equivalent) use any of the following to answer enquiries from the medical profession ?

   Reprints (or photocopies) of journal articles ☐
   Company reports (unpublished) ☐
   Sales promotion literature ☐
   Technical booklets * ☐
   Other literature - please state

   _____

* If YES, may I have a sample of a technical booklet (or equivalent). Please indicate whether it is intended for hospital doctors or general practitioners or both

   Hospital Doctors ☐
   General Practitioners ☐
   Both ☐

9. What information is sent to a member of the medical profession who has requested "full prescribing information" about a drug ?

   _____

10. Does the material sent depend on the enquirer's status, for example, whether he is a hospital doctor or a general practitioner ?

    YES ☐ NO ☐

    If YES, what factors affect the material sent ?

    _____

11. Are all the staff who answer enquiries equally able to cope with any query ?

YES ☐ NO ☐

If NO, why not ?

---

12. Would a reply to a request for specific information about one of your company's products usually include the same material that would be sent in response to a request for "full prescribing information", in addition to a letter answering the specific enquiry ?

YES ☐ NO ☐

If NO, in what way would it differ ?

---

13. How would you answer the following questions (in terms of what sources of information would you use) ?

1. Do you know of any adverse reactions likely to occur with the administration of you product..... ?

---

2. Do you know of any drug interactions likely to occur with the administration of your product..... ?

---

3. Please send me information to help me evaluate your product.....and compare it with a similar product marketed by a competitor.

---

14. How many enquiries did you receive last week ?

by telephone ☐
in the post ☐
from a representative * ☐

* on behalf of a recently visited doctor

15. Do some doctors write regularly for information ?

YES ☐ NO ☐

If YES, please state any specific characteristics common to these doctors, that you have noticed

---

16. What are the most common information requests that you receive ?

_____

17. What hours is your information service available by telephone ?

_____ a.m. to _____ p.m.

18. Do you have any additional facilities to cope with urgent enquiries received by telephone outside "office hours" ?

YES ☐ NO ☐

If YES, please state what arrangement exists

_____

19. How quickly would a

written request be answered ? _____

telephone request* be answered ? _____

* if not immediately because the relevant information is not to hand

20. Do you ever receive enquiries for over the counter drugs ?

YES ☐ NO ☐

If YES, please state in what way (if any) these enquiries differ from enquiries about prescription only medicines

_____

21. Does your department have any contact with your own company's representatives ?

YES ☐ NO ☐

If YES, please state

_____

22. What would you say the function of your department was ? (i.e. please state what work is carried out in your department)

_____

23. For company's that provide ONLY the data sheet in response to a request for full prescribing information

Does your company believe that the data sheet provides full prescribing information ?

YES ☐ NO ☐

If NO, why not ?

---

24. What factors determine which reprints of published articles are kept by your department for distribution to doctors in response to relevant enquiries ?

---

25. Does your information department (or equivalent) liase with any hospital drug information centres ?

YES ☐ NO ☐

If YES, to what extent ?

---

26. How do you view hospital drug information centres ?

---

27. Do you think that information staff in drug firms, in general, provide unbiased information on their company's products ?

YES ☐ NO ☐

If YES, how do you define unbiased ?

If NO, why not ?

---

28. Are the techniques of sales promotion the same for both hospital doctors and general practitioners ?

YES ☐ NO ☐

If NO, please describe the differences

APPENDIX5B

INFORMATION RESOURCE USED BY THE PHARMACEUTICAL INDUSTRY

Page No.

CONTENTS

1. Index Medicus is a monthly indexing publication divided into subject and author sections, both arranged alphabetically. Each article cited is given as many subject headings as is appropriate (the average is three) and is listed accordingly (as author, title and publication reference). The monthly issues are accumulated annually. Since 1970, the National Library of Medicine has issued a monthly Abridged Index Medicus, which cites articles from 100 English language journals, using the same subject headings as Index Medicus. This too is accumulated annually. The low cost of this index makes it a worthwhile proposition for small libraries.

The list of headings used is published annually as part 2 of the January issue under the title Medical Subject Headings (MeSH). This includes an alphabetical list of headings with cross references, categorised lists of headings and full information on new and altered headings.

2. MEDLARS (Medical Literature Analysis and Retrieval System), a by-product of the compilation of Index Medicus, Index to Dental Literature and International Nursing Index, is a computer data base. Each cited article receives more subject headings than appears in Index Medicus, averaging 12 per article for important journals. The editorials, letters, bibliographies and obituaries are indexed in the more important journals if substantive. Letters reporting adverse drug reactions are always indexed. Access to U.K. Medlars is via the British Library Lending Division, Boston Spa, Wetherby, Yorkshire, or via UKCIS (United Kingdom Chemical Information Service).

3. MEDLINE (Medlars on-line) is a by-product of MEDLARS. It is a data base containing citations appearing in the past three years of Index Medicus. There are supplementary files containing MEDLARS citations for preceding years and a SDILINE - (Selective Dissemination of Information) containing all citations for the current month of index medicus. (SDI describes the method whereby a computer regularly selects references from a broad data base which fit a previously defined interest profile and hence SDILINE can be used for monthly alerting searches).

The MEDLINE system operates under programmes written by System Development Corporation (SDC) and named ORBIT. Other on-line data bases are distributed by SDC.

4. BLAISE (British Library Automated Information Service) is an on-line, interactive, computerised information retrieval system. A range of medical data bases are available including MEDLINE, SDILINE, (latest month of the MEDLINE data base), CHEMLINE and TOXLINE and the MeSH vocabulary file. The on-line file holds references from 1975 to the present date. Older material is available for off-line searching. (TOXLINE is described below).

5. Current Contents is a fortnightly publication which includes copies of the contents pages (usually photographically produced) of particular journals. The two publications designed for medical literature coverage are Current Contents/Life Sciences (covering about 1,070 journals) and Current Contents/Clinical Practice (covering about 700 journals). Some sections of these

two publications have key word indexes to enable users to check for certain topics.

6. ASCA (Automatic Subject Citation Alert Mark IV) of the Institute of Scientific Information (ISI) is a current-awareness service, produced weekly from computer tapes used for the production of Science Citation Index (SCI) (see below). This service does not use subject word approaches described for use of Index Medicus, MEDLARS and MEDLINE but subject relationship in the content of papers citing other works as authorities. ASCA offers a multidisciplinary system drawing citations from SCI, Social Science Citation Index and a number of journals in Current Contents/Clinical Practice. The system indexes about 520,000 articles each year from 5,200 primary journals, of which approximately a third are bio-medical. ASCA tapes can be searched by using the author's name (to retrieve articles he publishes), the author's published work (to retrieve papers citing this work), the organisation (to retrieve papers published by other workers in an organisation), in addition to conventional searching by word fragments, phrases and words.

A recent development of this service is ASCATOPICS, a series of weekly ASCA profiles of fixed topics. Ninty such topics are available in the medical sciences, 91 in general life sciences and 51 in pharmacology. Individually requested profiles are also provided. ASCA is available in the U.K. by ISI European Branch, 132 High Street, Uxbridge, Middlesex.

7. Science Citation Index is a quarterly publication for retrospective searching. It is accumulated annually. It consists of a

list of references (cited works) in which each reference is followed by a list of sources (citing works) which quote the original reference. In 1976, about 2,400 journals provided "sources" of articles.[1]

Each issue contains,

a. a citation index listing references under authors' names and under each reference, authors and articles that have cited it, plus bibliographical details;

b. a list of institutions to which indexed authors belong;

c. a source index listing authors whose articles have had their citations indexed;

d. a 'Permuterm' index which provides a subject guide to the source index. (This index is completely permuted for every important word of the title i.e. the title of the paper is indexed under every other important word in the title. This leads to redundancy and hence the context of the terms being searched for should be checked).

8. TOXLINE is produced by the National Library of Medicine and provides citations on toxicology and environmental effects of chemicals and pollutants. It contains the American Society of Hospital Pharmacists' - International Pharmaceutical Abstracts, Chemical Abstracts Services' - Chemical - Biological Activities, Biosciences Information Services - Health Effects of Environment Pollutants (HEEP), MEDLARS - Toxicity Bibliography and Environmental Protection Agency's - Pesticides Abstracts (PESTAB).

The TOXLINE data base is available on-line using Lockheed

Information Retrieval Systems. The service is available using RECON programmes. In the U.K. the service is offered by UKCIS and the U.K. MEDLARS Service. The file contains 320,000 citations from 1971 onwards. TOXBACK is another file containing 190,000 citations from 1965 to 1970. Each record in the data base has full bibliographic details plus an abstract and/or index terms and chemical abstracts service registry numbers.

9. The Excerpta Medica Foundation produces 40 English language abstract journals covering different subject areas in the whole field of biomedicine. It is intended for the physician and abstracts from 3,500 biomedical journals, 200 chemical journals and 50 physics journals. Although its coverage is greater than Index Medicus, the number of articles abstracted is slightly lower because of greater selectivity.

The computer data bank used for the production of the abstract journals provides several by-products, two of particular interest in drug therapy. These are Adverse Reaction Titles - an index of all papers on untoward effects of drugs or chemicals and Drug Literature Index - an index by generic name, brand name and activity class to papers which involve drugs. (No abstracts are provided; these publications list title and keywords only). The Drug Literature Index is very useful for retrieving papers on drugs which are not well known and difficult to trace in Index Medicus.

The computer tapes are available weekly for current awareness and retrospective searching. The standard service contains abstracts in addition to classification categories, subject headings and item index codes. However the needs of

the individual subscriber can be catered for and tapes containing different amounts of information provided accordingly. A partial subscription to computer tapes is DRUGDOC which gives high priority to drug-related information. Citations can appear within eight weeks of receipt of the original article. In addition DRUGDOC tapes contain information for each citation under the generic name of the drug (or chemical name or equivalent, if no generic name exists), the brand name, name and location of the manufacturer, the chemical structure, clinical indications and contraindications and clinical and pharmacological effects and adverse reactions.

Informatics Inc. are making the Excerpta Medica tapes available on-line, using RECON programmes via Lockheed Information Retrieval Systems.

10. RINGDOC is a service intended mainly for the industry and is produced by Derwent Publications Ltd. of London. It provides about 50,000 informative abstracts from more than 400 journals per year. The abstracts average 250 words in length and contain full bibliographic details. They are preceded by a summarised statement comprising key words which facilitates scanning and retrieval. The abstracts are provided weekly in batches of punched cards (approximately 650 double sided cards) or monthly, as computer tapes for the house retrieval. Alternatively, abstracts are available in SDI profile booklets, from a possible list of 42 profiles.

On-line access is available via SDC to enable retrospective searches to be made back to 1964.

Derwent Publications also provide FARMDOC which is an index to drug patents, VETDOC for veterinary literature and

PESTDOC for pesticide references.

11. BIOSIS (BioSciences Information Service) publishes Biological Abstracts and Bioresearch Index. The cited articles are indexed by the KWIC (Keyword in Context) system. To retrieve a reference, only the key word or index term needs to be known. This will appear in the centre of a column, with part of the title before and after it. About 7,700 journals covering biology, experimental medicine and public health are covered.

BIOSIS provides its source tapes to various organisations, it also produces HEEP which is part of the on-line TOXLINE data base.

12. International Pharmaceutical Abstracts (IPA) provides abstracts of publications dealing with pharmaceutical technology, adverse drug reactions, toxicity, investigational drugs, drug evaluations, biopharmaceutics, pharmaceutics, drug stability, pharmacology, chemistry, drug analysis, drug metabolism, and body distribution, pharmacognosy, legislation, laws and regulations, sociology, economics and ethics and pharmaceutical education. It is produced by the American Society of Hospital Pharmacists and provides about 5,000 abstracts per year. From its data base,it offers printed services, microform publications, computerised searches and bibliographies. It has also published "Drug Interactions 1 and 2" which are computations of all articles on drug interactions during 1970 to 1972 inclusively, together with abstracts and an index.

IPA since 1970 is available as part of TOXLINE.

13. Chemical Abstracts is a weekly publication abstracting from biochemical, organic chemistry macromolecular chemistry, applied chemistry, chemical engineering, physical and analytical chemistry journals. UKCIS, the computer based current awareness and retrospective services system uses the computer tapes which produce Chemical Titles and Chemical Abstacts.

14. Other Abstracting Services

a. Clin Alert is an abstracting service providing information about unusual occurrences in the use of therapeutic agents and procedures. It is a useful source for reports of adverse drug reactions and it includes complete bibliographic details.

b. Midas is a specially designed system developed for use by ICI Pharmaceuticals Division. Its aim is to provide a comprehensive information service on ICI products and their direct competitors. Information is drawn from 6,000 medical pharmacological, biochemical, veterinary and chemical journals published worldwide. The system is described in detail by Haygarth-Jackson.[2]

15. Index of New Products is a card system published by the Pharmaceutical Society of Great Britain. Each card (indexed by brand name) lists chemical composition, presentation, action, indications, dosage, overdosage and treatment, special (medical) precautions, side effects, compatability with other products, cost, supplier (or manufacturer), legal class, product licence number and date of introduction. The same information is also published in the Pharmaceutical Journal (excluding date of introduction) under "Drugs in Use".

16. de Haen Services provide a comprehensive indexing service to medical and drug literature. The abstracts are provided on 3" x 5" cards.

Drugs in Use and Drugs in Combination are a combined card service covering drugs actually marketed. The cards contain the same type of information in approximately the same place e.g. age and sex of individuals studied always appear in the left hand column. This facilitates scanning. About 5,000 cards are issued per year.

Drugs in Prospect provide the first announcement of new therapeutic entities and list the following twelve items of information:- therapeutic, pharmacologic and chemical classes, location of study, molecular formula, names (brand and generic) and code numbers (if available), experimental design, inverted chemical name plus author, title and journal citation. Approximately 2,000 cards per year are issued.

Drugs In Research cards cover papers which occur between discovery and marketing of a product. About 2,500 per year are produced.

The de Haen services cover 400 journals per year and about 50% of these are English language publications.

17. Unlisted Drugs is a monthly journal identifying and describing all newly reported drug compounds and products which are not listed by name, manufacturer and composition in the latest editions of main drug reference compendia (American Drug Index, Merck Index, Martindale's Extra Pharmacopoeia etc.). Entries include name (brand and generic), composition, manufacturer activity (pharmacological or clinical), bibliographic references, structural formulae of newer compounds, other names for the same

preparation by the same manufacturer, recommended dosage, synonyms and earlier un-listed drug references to other names for the same drug may be included. All entries are also available on 3" x 5" cards as a separate service containing all drug identifying information.

18. Textbooks

Two textbooks in particular were mentioned:

a) AMA Drug Evaluations

The American Medical Association's publication is an authorative reference book which includes discussions about new drugs, generic and proprietary names, structural formulae, available preparations, side effects, adverse effects, contra-indications and drug interactions.

b) Martindale's Extra Pharmacopoeia

Martindale's Extra Pharmacopoeia published by the Pharmaceutical Society of Great Britain contains monographs, each stating the generic and chemical name of a product, its recommended dosage, pharmaceutical precautions, toxic effects and treatment, absorption and fate, clinical uses and available branded preparations. The 1977 edition covered more than 5,600 products.

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APPENDIX 5C

LIST OF SUBJECT CATEGORIES USED TO ASSESS SUBJECT COVERAGE BY COMPANIES JOURNAL HOLDINGS LISTS

The subject categories were based on the list of medical specialities in the Health and Personal Social Service Statistics for England, 1976, published by the Department of Health and Social Security. The subjects include the following:

Anaesthesiology
Cardiology
Clinical Pharmacology and Therapeutics
Dentistry and Oral Surgery
Dermatology
Diseases of the Chest
Ear, Nose and Throat
Endocrinology
Gastroenterology
General Medicine
General Surgery
Genito-Urinary Medicine
Geriatrics
Gynaecology and Obstetrics
Haematology
Immunology
Infectious Diseases
Nephrology
Neurology
Nuclear Medicine
Ophthalmology
Paediatrics
Pharmacy
Psychiatry
Rheumatology and Rehabilitation
Radiotherapy
Radiology
Thoracic Surgery

Traumatic and Orthopaedic Surgery
Tropical Medicine
Urology
Venerology

APPENDIX 5D

INFORMATION CONTAINED IN THE TECHNICAL BOOKLETS

INTRODUCTION

Technical booklets were used by the majority of the firms participating in this study to answer enquiries from members of the medical and pharmaceutical professions. Since they are so widely used, a study of the information that they contained was carried out.

Technical booklets were defined as product guides which were designed to provide prescribing information.

METHODS

1. The Sample

At least one technical booklet was provided by 90% of the firms visited. If more than one was supplied, the booklet describing the most recently launched product was selected for analysis, because it was assumed to represent current policy concerning the provision of information. In two cases, two technical booklets for the same product were provided, one designed for hospital doctors and the other for use by general practitioners. In both cases, the information contained in the booklet designed for hospital doctors was included in the analysis.

2. Analysis of the Information Content

A checklist was prepared to assess whether the items of

information that a sample of hospital doctors considered of basic importance to prescribing (see Chapter 2) were included in the technical booklets. They were expected to provide the following information about the product that they were describing:

1. the approved name, chemical name or formula;
2. the indications;
3. the adult, geriatric and paediatric doses;
4. the strength of all presentations;
5. the route, frequency and timing of administration;
6. the contraindications;
7. special precautions which were expected to include details of teratogenic effects, effects of sudden withdrawl, the storage instructions and shelf life;
8. adverse drug reactions and side effects, which were to be listed in headed sections in the booklet. The adverse reaction section (ADR) was to include:
   a. incidence;
   b. severity of reactions described;
   c. action to be taken if reaction was severe;
9. the usefulness or efficacy which was required to include details of the mode of action, the necessary duration of therapy before the desired effect occurred, and reports of referenced clinical trial reports. The mode of action was assessed by the presence of details about:
   a. the site(s) of action of the drug (e.g. type of tissue etc.);
   b. the effect of the drug (or its metabolites) on the sites of action;

c. the result of the action on the target site(s).

Referenced reports of clinical trials were identified by the following descriptors: trial, double-blind study, single-blind study, placebo-controlled study, and comparative study. Referenced reports were those that were published in medical journals and symposia proceedings. The descriptions of trial reports were expected to include all the information that the summary of the published article was required to state (see Chapter 3, Appendix 3A);

10. treatment of overdosage;
11. drug interactions which were to be included in a headed section in the booklet;
12. presentation which was to list details of all types of presentation (e.g. tablet etc.), colour and package quantities;
13. the cost of all presentations in the various package quantities;
14. the absorption and distribution of the drug in the blood and body tissues, and the excretion of the drug. The absoption was expected to be included as a headed section in the booklet and to state:
    a. the method of absorption of the drug into the body;
    b. whether or not the drug crossed the blood-brain barrier and the placenta;
    c. whether or not the drug is absorbed into the cerebrospinal fluid and the maternal milk.

The distribution was to be included as a headed section and to state:

a. the time taken for the drug to reach therapeutic levels in the blood;

b. the duration of action of the drug;

c. the concentration (or percentage) of the drug reaching the desired site(s) of action;

d. the percentage of the drug that is metabolised.

The excretion was also to be included as a specific headed section and to list:

a. the main method of excretion;

b. the main form of the drug when it is excreted (i.e. as unconverted drug or metabolites);

c. the percentage of the main form that is excreted by the main method.

To simplify the presentation of the data, if a particular item of information was either implicit in the text, or was not relevant to the description of a particular product, it was considered to have been mentioned. This was to avoid presenting three categories of results, one for data included, one for data that was not relevant, and one for data that was absent.

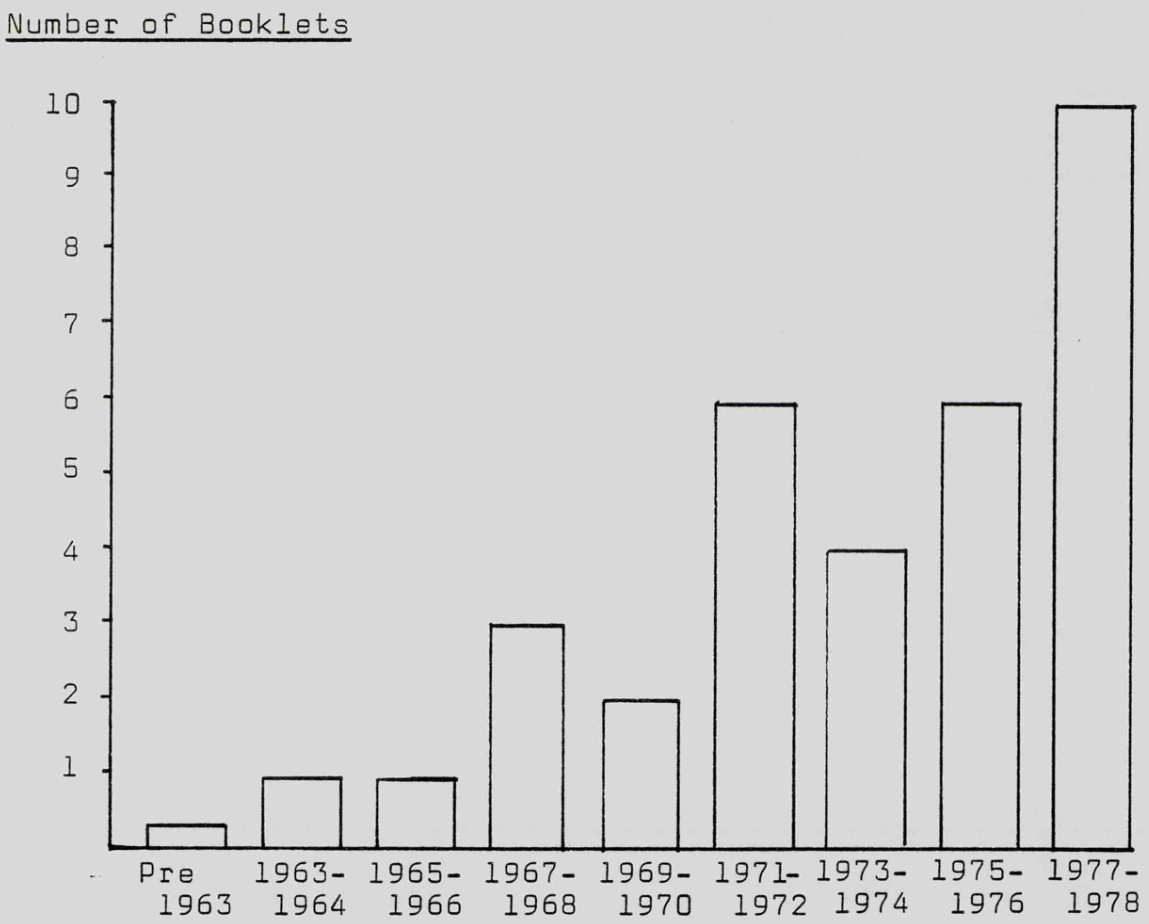
RESULTS

1. General Characteristics of the Sample

The majority of the booklets that were analysed described products that had been introduced on to the market since 1971 as shown in Figure 1 (see page 203). The date of introduction was obtained from the Index of New Products published by the Pharmaceutical Society of Great Britain.

FIGURE 1

DATE OF THE LAUNCH ON TO THE MARKET OF THE PRODUCTS DESCRIBED IN THE TECHNICAL BOOKLETS



2. Information Content of the Technical Booklet

The information content of the booklets is shown in Tables 1 and 2 (see pages 205 and 206). There was no significant difference in the information contained in booklets describing products which were marketed before and after 1972. In addition, there was no difference in the information provided in the booklets describing products which act mainly on the cardiovascular system (9 products), the central nervous system (9 products), infections (7 products) and other parts of the body (11 products).

DISCUSSION

Since technical booklets are usually provided together with a data sheet, the inclusion of the information contained in the data sheet in the technical booklet is not strictly necessary. The data sheet, however, does not include details about product efficacy, drug interactions, cost and the absorption and distribution of the drug in the blood and body tissues and excretion of the drug. It appears that the majority of technical booklets also fail to provide this information.

Although 83% of the booklets made reference to reports of clinical trials, the information that the booklet provided in the description of the reports was very limited. Only 54% stated the result of the trials. This suggests that inclusion of a referenced report was a promotional tactic, and the published work is used as a recommendation in itself, regardless of the content of the actual article.

TABLE 1

INFORMATION CONTENT OF TECHNICAL BOOKLETS

Items of Information Mentioned			% of booklets containing information
1.	Approved name		97
	Chemical name or formula		86
2.	Indications		97
3.	Dose	- adult	100
		- paediatric	61
		- geriatric	28
4.	Strength of all presentations		100
5.	Administration	- route	86
		- timing	33
		- frequency	92
6.	Contraindications		83
7.	Special precautions	- teratogenicity	58
		- effects of with withdrawl	14
		- storage conditions	33
		- shelf life	8
8.	Adverse effects	- adverse effects section	28
		- side effects section	78
		- incidence of ADR	36
		- severity of ADR	47
		- action if severe (ADRs)	47
9.	Efficacy	- mode of action	53
		- duration of therapy	28
		- containing clinical trial reports	83
10.	Overdosage treatment		47
11.	Drug interactions		25
12.	Presentation	- all types	89
		- colour of all types	56
		- package quantities	83
13.	Cost		17
14.	Absorption	- section	36
		- method of absorption	22
		- crossing blood brain barrier	19
		- crossing the placenta	22
		- into the cerebrospinal fluid	11
		- into maternal milk	14
	Distribution	- section	22
		- time to therapeutic levels	64
		- duration of action	64
		- amount reaching site of action	28
		- amount metabolised	19
	Excretion	- section	42
		- main method	67
		- main form	61
		- amount of main form in main method	58

TABLE 2

INFORMATION CONTENT OF TRIAL REPORTS AS DESCRIBED IN TECHNICAL BOOKLETS

Information Mentioned	% of trial reports described in booklets
Name of the trial drug	96
Type of action it possesses	31
Disease the drug was treating	69
Number of patients on the trial	77
Dosage schedules used	55
Duration of therapy	56
Design of the trial	43
Results of the trial	54
Significance of the results	30
Generic name of the drug	33

It was noted that it was very difficult to find some items of information in several of the technical booklets, because they did not include either a contents page or an index. This would probably be a valuable addition to these booklets.

Several of the booklets described the disease that the product was intended to treat. However, as this information was not considered to be of importance to basic prescribing (as assessed by hospital doctors), and there was no standard format to the presentation of this section of the booklet, no attempt was made to measure the information it contained.

It was not possible to assess whether each booklet was a promotional device, because this would depend on the way in which it was used and also the information requirements of the recipient. It appears that, in general, technical booklets do not fill the gap between the information provided by the data sheet and the information that hospital doctors require, despite being an excellent means to do so.

APPENDIX5E

DETECTING ADVERSE DRUG REACTIONS - THE CURRENT DEBATE

The recognition of the occulomucocutaneous syndrome, associated with the drug practolol, is the most recent of the unexpected and serious adverse drug reactions to be reported. This syndrome is characterised by a rash, eye lesions, secretory otitis media, scherlosing peritonitis, pleurisy and pericarditis.[1] It was only detected after four years of marketing and occurred despite attempts to avoid another "thalidomide disaster". Regulatory bodies have relied on the medical profession to report adverse drug reactions on a voluntary basis. The failure of this system and the concern about the toxicity of other drugs have prompted discussion about new methods for monitoring adverse effects.

Definitions

Controversy surrounds almost every aspect of detection of adverse drug reactions (ADR), but perhaps the most fundamental problem is the definition of an ADR.

The World Health Organisation (WHO) define a drug as,

> "any substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient." 2

An ADR is any response to a drug

> "which is noxious and unintended, and which occurs at doses used in man for prophylaxis, diagnosis, or therapy."2

Napke,[3] considered that this definition should include lack of therapeutic effect, but Karch and Lasagna[4] strongly disagree

with this view. Several different authors,[5-9] have used other definitions of ADRs in studies of the epidemiology of ADRs, whilst other authors,[10,11] used the term without any definition.

Inclusion of side effects with ADRs provides a further complication, because the distinction between a side effect on an ADR is not precise, nor scientifically based.[12] (Side effects are usually restricted to therapeutically undesired but unavoidable effects. Koch Weser et al[9] suggested that they should be excluded from the definition of an ADR when they are "trivial and expected".)

The conclusion reached by a recent drug monitoring symposium[13] stated that there is a need for a common drug and adverse reaction terminology. This could be extended to include the need for clarification of the status of side effects and therapeutic failures.

Reasons for the Occurrence of Adverse Reactions

ADRs occur because the preparation of a product for marketing does not permit accurate predictions of use in large human populations to be made. The following list explains some short-comings of the present system:

1. animal toxicity studies do not always bear a relationship to eventual human hazards;
2. clinical trials may not demonstrate full ADR potential, particularly if the reaction has a very low incidence, because the rate of exposure to humans is low at this stage;
3. reactions with long latent effects may be missed during comparatively short exposures to a product,

in the clinical trial phase of drug testing;

4. the population taking part in a clinical trial may be very different from the population that will eventually use the drug after marketing. This can occur, for example, by deliberately selecting patients in the 20-60 age groups or those who have only the disease being treated by the test drug;
5. the reactions due to drug interactions may be missed if patients taking part in a clinical trial are requested to avoid all other forms of medication.

Reasons for the Lack of Detection of Adverse Reactions

One major reason for the lack of detection of ADRs is the difficulty in connecting cause with effect.[14] This is particularly difficult if the ADR is clinically manifested in the same way as patient deterioration due to the disease process, or if other drugs were being taken concurrently.

Drury[15] lists five factors affecting the recognition of ADRs. These include:

1. the lack of knowledge of pharmacology which prevents the doctor from suspecting that an ADR has occurred;
2. the difficulty in diagnosing and separating a possible ADR from other diseases;
3. the denial by the doctor that his therapy (decision) has caused an ADR;
4. the lack of time available for recognition of an ADR because the time for each patient consultation is very short;
5. patient factors, for example, patients not reporting adverse effects or doctors ignoring patients who

complain frequently about their treatment.

Neither Crooks or Drury suggest any solution to the problems of lack of detection of ADRs. However, post-graduate education in all aspects of clinical pharmacology together with increasing the length of time available for each patient consultation could solve the majority of the problems mentioned by Drury. Those discussed by Crooks are more fundamental to the concept of an ADR.

Method of Post-Marketing Surveillance

There are two basic methods of monitoring ADRs using post-marketing surveillance techniques. These are monitored release and registered or recorded release.

1. Monitored Release

Several methods of monitored release are currently in operation. They include the following:

a) Spontaneous Reporting

This usually occurs in letters or case reports published in journals and in lectures or discussions at meetings or seminars. This method is poor for rapid dissemination of information and there is no possibility of evaluating ADRs reported in this manner.

b) Voluntary Reporting

Voluntary reporting systems exist in the U.K., the U.S., Canada, Sweden, Australia, West Germany, New Zealand and the Netherlands. They rely on health care professionals to report confirmed and suspected ADRs. In the U.K. the system was established in 1964, and reports are received on specially designed yellow cards. The reports are reviewed twice a week

by medical staff and are prepared for coding. Part-time field workers are responsible for evaluating particular cases. The advantages of the system are in its coverage of the total population and its low operational costs. The disadvantages, however, are many and include:

1. under-reporting;
2. variation in the quality of data provided (inadequate data are very costly to follow up);
3. biases in the reporting due to excess publicity, e.g. special requests to report adverse effects occurring with particular drugs etc. These factors tend to distort actual incidence of occurrence.

Under-reporting has attracted a great deal of criticism. It has been estimated that only 1 - 10% of adverse reactions occurring are reported to the Committee on Safety of Medicines (CSM) using the yellow card system.[16] Inman has identified

> "the seven deadly sins of doctors - complacency in the mistaken belief that only safe drugs are marketed, fear of litigation, guilt about damage to patients, ambition to publish a personal series of cases, ignorance about what should be reported, diffidence about reporting mere suspicions, and plain old fashioned lethargy." 17

Crooks adds to this list pressure of work, lack of motivation and "administrative defects" e.g. the yellow card not being to hand.[14] Drury comments that many general practitioners are unwilling to become involved if there is a possibility that they would be required to answer further enquiries.[15] Not surprisingly, since the majority of patients receive prescriptions from general practitioners, the general practitioner is the major source of reported ADRs in the U.K.[18]

Table 1 (see page 213) shows the number of ADRs reported to the CSM between 1972 and 1976.

TABLE 1

NUMBER OF REPORTS OF ADVERSE DRUG REACTIONS RECEIVED BY THE COMMITTEE ON SAFETY OF MEDICINES

Year	No. of ADR reports
1972	3638
1973	3619
1974	4818
1975	5052
1976	6490

Source: Annual Reports of the CSM.

c) Intensive Hospital Monitoring

This method of post-marketing surveillance requires doctors, nurses and pharmacists to monitor a defined patient population for ADRs. The most successful system, to date, is the Boston Collaborative Drug Surveillance Programme which has monitored 19 hospitals in six countries. A nurse monitor (trained in ADR detection) collects detailed patient data on a daily basis. These data are assessed by a medical team and fed into a computer. The output is analysed by an expert team of clinicians, epidemiologists, biomedical and statistical staff to determine the incidence of ADRs and to detect unsuspected reactions and interactions.

Lawson[19] reports very similar reaction rates in the USA, Italy, Israel and Scotland for medical in-patients and

suggests that further studies in different hospitals are of limited value as the results are generally applicable.

The advantage of this system is its independence of clinical judgement on casual relationships. The disadvantages are its high cost (salaries of skilled team members), the limited number of patients monitored, and the collection of data on specific wards (and, therefore, a specific population is monitored which may be atypical of the whole population).

Other surveillance systems have been developed by the Aberdeen-Dundee Medicines Evaluation and Monitoring Group, by the Duquesne University School of Pharmacy, at Stanford University (for drug interaction detection and prevention) and at the University of Melbourne, St. Vincents Hospital, Australia.[14]

d) Case Control Surveillance

Despite the obvious value of intensive monitoring of ADRs occurring in in-patients, concern was expressed about the events which escaped detection, due to lack of information about previous drug consumption and the short follow up surveillance (on average about 10 days, by the Boston Collaborative Drug Surveillance Programme). When these data were collected, processed and added to the data obtained using the intensive hospital monitoring system, case control surveillance was possible. A patient, a drug or an adverse effect could be studied singly or in combination with matching controls. The advantage of this type of surveillance is its ability to identify and assess retrospectively specific problems.

The disadvantages are its cost, (although once set up and data collection procedures have become routine, the cost would diminish rapidly[20]), and the problems associated with the

recall of previous drug therapy by patients.

e) Record Linkage

This form of monitoring involves collecting the complete medical records of individual patients. Such a system exists in Finland and has been described by Idänpään-Heikkilä.[21] The advantages include the following:

1. nation wide data are collected;
2. it is a relatively cheap method of data collection;

and in the case of the Finnish system, additionally:

3. the informants (doctors) belong to a national care system and notification to some of the registration bodies such as the Cancer Registry and the Register of Congenital Malformations (to drugs) etc. is already compulsory;
4. information forms are part of the medical record, and must be completed before the patient can receive reimbursement of the cost of the drugs prescribed;
5. the Social Security number allows linkage between the registries and the original medical records (because it identifies each individual).

The disadvantages of the record linkage system are:

1. the necessity to expose a large enough population to a drug before detection and evaluation of ADRs can occur;
2. the lack of uniformity in the data collected, both in the terminology and the expression of medical facts by individual doctors. Skilled staff are required to code the data;
3. the difficulty in ensuring that the data are complete;
4. the lack of records which include details of each

patient's self medication.

f) Compulsory Monitoring

This requires doctors to report ADRs by law. Such a system exists in Sweden, but reporting has been restricted to serious ADRs, death and reactions prolonging treatment in hospital. The actual value of this system is not yet known.

The advantages include a high rate of reporting[22] and the heightened awareness among the medical profession of the importance of detecting ADRs. The disadvantage is the effect of compulsory reporting on clinical freedom.

g) Regulatory Monitoring

This requires all manufacturers to keep a record of all adverse reactions to new drugs. In some countries (the U.K. included) this information must be passed on to the regulatory authority shortly after notification. However, in the U.K. some companies have been suspected of "dragging their feet" in reporting ADRs, particularly in the case of unconfirmed reports.[23]

An advantage of this method of monitoring is the possibility of avoiding the unwillingness of doctors to write a report for the CSM. ADRs are reported to medical representatives or to pharmaceutical firms directly.

h) International Monitoring

The World Health Organisation has established an international collating centre for suspected and confirmed ADRs. This centre offers an opportunity for national differences and similarities in the responses to drugs to be studied.

To overcome the deficiences in the various methods of monitored release, several systems which will measure the actual

incidence of ADRs in large populations have been proposed. These systems use the basic concept of registered release.

2. Registered Release

Dollery and Rawlins[23] and Inman[24] independently suggested similar schemes for ADR monitoring. Both authors proposed that certain drugs should only be available for prescription if doctors submitted records of their use to a regulatory body.

On average, about 2,000 patients have been exposed to a new drug when it is cleared for marketing in Britain.[25] The post-marketing surveillance suggested by Dollery and Rawlins and Inman would require the reporting of all reactions occurring in a further 10,000 or 100,000 patients.

Early experiments using this concept of registered release have been carried out by individual pharmaceutical companies, using their own methods of collecting information. Not only did they find difficulty in encouraging doctors to complete report forms, but also the information received did not detect any new side effects of clinical importance. Unfortunately, financial incentives (and calculators, stethoscopes etc.) used by some companies to encourage doctors to complete report forms, debased the aim of registered release and the scheme degenerated into a promotional trial.[23] The average cost was about £100 for every patient monitored.[25]

Dollery and Rawlins[23] proposed that registration documents should be distributed to doctors, probably most efficiently by medical representatives. Registration would occur when the doctor completed a four-part document which would contain the following information:

1. a serial number;

2. the drug name;
3. the date of commencement of therapy and the dose prescribed;
4. the diagnosis;
5. the NHS number of the patient;
6. the name, address, sex and date of birth of the patient;
7. the name and address of the registering doctor.

The doctor would keep the top copy and the other three would be distributed as follows: one would be sent to a registering agency, one to the Office of Population Censuses and Surveys (OPCS) and one to the pharmaceutical company involved. This last copy would contain only the serial number, drug name and NHS number of the patient, to preserve the confidentiality of the patient.

The registering agency would distribute questionnaires to both the doctors and the patient at regular intervals for a period of time (e.g. once a year for five years). Dollery and Rawlins suggested that patients should be informed that they were to be prescribed a drug on registered release. The questionnaire to the doctor would ask him to state whether the patient was still receiving the drug, and all diagnoses and hospital referrals made during the previous year. The questionnaire to the patient would ask the same question, plus details about "many different bodily systems and symptoms".[23] The OPCS would report deaths of monitored patients for up to 20 years afterwards.

Dollery and Rawlins proposed that new chemical entities should always be registered. They also suggest that fees should be paid to doctors (£2.50 for initial registration and

£1.00 per follow up). The registering agency could be administered by a professional group (e.g. the Royal College of General Practitioners, or the Royal College of Physicians), because it was felt that doctors would prefer to avoid reporting to a government body.

Many objections to this scheme have appeared in the medical press. Wilson[26] felt that the extra work created for the prescribing doctor was the main drawback of the scheme. He also objected to the proposed constraints on the promotion of a new drug for general use, until the required number of patients has been monitored. Both of these factors could cause the registered population of patients to be atypical of subsequent users.

Drury[27] objected to involvement of patients in the monitoring scheme, because he felt that this would adversely affect the doctor-patient relationship. Lawson and Henry[28] indicated several problems in the scheme proposed by Dollery and Rawlins. These included the following:

1. the cost of reporting, if borne by the manufacturer, would increase the cost of drug development and new drugs;
2. the distribution of registration documents by medical representatives was unsatisfactory because they would have a vested interest in the outcome of the monitoring;
3. legislation to prevent the dispensing of prescriptions to patients who were not registered would be required, and this would add to the cost of the scheme;
4. the monitoring programme might alter the prescribing habits of general practitioners and this would result

in a population atypical of subsequent users;

5. involvement of the patients in the monitoring might cause unnecessary anxiety, if they thought that they were being used as "guinea pigs";
6. The fear that the CSM might slaken the pre-marketing requirements if they knew that a drug would be subjected to post marketing surveillance.

Lawson and Henry suggested that monitoring could be carried out by pharmacists, who would identify patients receiving particular drugs and pass the information that is already recorded on the prescription form to a registration body. (This information includes the name of the patient, his age group, address and a number which identifies the prescriber.) The registration body would be responsible for monitoring particular patients by asking the prescriber if the patient had died, been admitted to hospital or referred to a hospital out patients department.

The scheme proposed by Inman[24] involved the use of a recorded drug package. This would contain three documents; one, a prescription form that could be easily identified by a pharmacist and the Prescription Pricing Authority (PPA); the second, an exact copy of the prescription which would be sent to the monitoring centre on the day of issue; and the third, a questionnaire to record ADVERSE EVENTS (rather than ADRs). (The PPA handles all prescriptions dispensed in the U.K. and is the body which reimburses pharmacists.) The questionnaire would also record details of the reasons for any further consultations, referrals to hospitals or to other doctors, and cause of death if this occurred during the monitoring period. Throughout this time, suspected ADRs would be reported

using the yellow card system. Drug packages would be issued by the monitoring agency.

Inman felt that the manufacturer should be allowed to receive data obtained from the reports. He was not sure whether patient involvement would be beneficial to the monitoring. Again linkage with the OPCS was proposed to record long-term drug effects that may result in death.

Reporting of adverse events was first advocated by Finney[29] for monitoring drugs after marketing. He defined an adverse event as a

> "particular untoward happening experienced by a patient, undesirable either generally or in the context of his disease". 29

Skegg and Doll[30] further support the need for information on adverse events and suggest that it should be extended to the clinical trial stage of drug development.

Wilson[26] also criticised the scheme proposed by Inman, because he felt that the use of special prescription forms to prescribe monitored drugs would alter prescribing habits and produce an atypical population of patients. Dollery[31] had doubts about the ability of general practitioners to remember to use special prescription forms for certain products. He did acknowledge that the system could work if pharmacists refused to dispense prescriptions that were incorrectly presented to them.

Wilson[26] has proposed a scheme that would avoid identification of a monitored product at the prescribing stage. It relies on identification of these prescriptions by the PPA. Photocopies of these prescriptions could be supplied to a registering agency. The data bank created could be used for retrospective searches if yellow card reports alerted the CSM to the

possibility of a serious reaction. In addition, at regular intervals, information about possible drug related effects could be elicited from prescribers in a questionnaire survey. Since Skegg et al[32] and Smithells[33] have used data provided by the PPA to investigate prescribing habits and adverse reactions to drugs respectively, this scheme provides a feasible alternative to monitoring by the prescribing doctor.

Brewer[34] noted that this scheme, in common with others proposed, requires the cost of monitoring to be borne by some other body than the institution to which the author belongs.

Factors Affecting the Success of the Monitored or Registered Release Programmes

1. Incidence Rates in Perspective

None of the schemes proposed for registered release indicate how comparison of drugs taken with suitable controls could be carried out.[35] Crombie[36] stated that the potential for testing suspected relationships between particular drugs and morbidity already existed in disease indexes that were maintained by more than 100 general practitioners, at the Research Unit of the Royal College of General Practitioners.

2. Human Judgement

Concern about the reliability of judgements of untoward clinical events has been expressed by Koch Weser.[37] He reported a study in which three clinical pharmacologists independently assessed 500 ADRs. The wide divergence of judgements indicated that the causative role of drug therapy in an adverse clinical occurrence is mainly a matter of opinion.

Hammond and Joyce[38] have identified other areas where human judgement affects reporting of ADRs. These include:

a. false association of effects of drugs with effects in patients;

b. the tendency to judge effects by considering their relative position in a previously learned range;

c. lack of consistency in the application of particular policies concerning ADRs.

It appears that variations in human judgement are inevitable.

3. Imprecise Methodology

Dollery[31] stated that the objectives of an ADR warning system was easy to formulate but difficult to achieve. There appears to be a growing opinion which suggests that "everything" should be recorded, in the hope that the computer will find potential ADRs. Since the computer must be programmed to look for possible effects this approach is probably not very valuable.

4. The Role of the Patient

Patient involvement is an essential part of the scheme proposed by Dollery and Rawlins.[23] Although Drury[27] felt that this would adversely affect the doctor-patient relationship, Howie[39] supported the concept of patient involvement, on the basis of a study that he had conducted. Hammond and Joyce[38] indicated that patient compliance can seriously affect the assessment of ADRs. Non-compliance can result in either the effect occurring at a dose lower than that reported, or the effect being due to another drug being taken. Patient involvement might reduce errors arising from these sources.

Lesser[40] proposed that patients who were prescribed a new drug should initially be given a week's supply. During this week, they should record any unusual reaction and be urged to seek advice if any observation caused them to be concerned. Continued therapy with the drug could only occur after consultation with the prescriber, when the report could be discussed. Although this proposal only attempts to provide short term surveillance, it could perhaps be extended to observe long term effects of drugs.

The major drawback to patient involvement is the "frightened guinea pig syndrome". If the public were educated about the benefit-to-risk ratio of taking any medication, this fear could possibly be overcome.

5. Reporting of Known Adverse Drug Reactions

Inman stated that he would

"hate to deal with a million ampicillin rashes each year" 41

This comment indicates the problems in reporting fairly common ADRs. Unfortunately the CSM in the U.K. does not issue any guidelines on the reporting of well known ADRs.

6. Liability

Doctors prescribing new drugs which would be available only using the registered release scheme, could be exposing patients to less of a risk than at present. The close contact that a doctor would have with a registering agency would enable rapid feedback of information derived from the records of all other participants.[24] Linking of the registered release scheme with "no fault" liability remains a subject for discussion. Recently

the Royal Commission on Civic Liability and Compensation for Personal Injury published a detailed report, but it recommended that the "no fault" scheme should not be applied to medical accidents.[42] A leading article in the British Medical Journal[43] reported that the Commission seemed to be more concerned about the difficulties in proving the cause of the accident, than the repercussions of successful action on a doctor's reputation.

The volume of discussion in the medical press makes a summary of the current debate concerning the detection of ADRs a very difficult task.

All monitoring methods currently being used have made valuable contributions to drug safety. The failure of the British systems to detect the serious adverse effects caused by practolol highlighted the need to improve and develop new methods of post-marketing surveillance.

The proposed methods of registered release aim to determine, as quickly as possible, whether a drug has an acceptable level of safety in relation to efficacy. It has been suggested that this form of surveillance should be reserved for new chemical entities that have shown no specific hazards in the pre-marketing testing.

The success of the record-linkage system used in Finland if of particular interest to those attempting to develop an improved monitoring system in Britain. As the majority of health care is carried out in the National Health Service, the potential for developing a similar scheme already exists.

Finally, the drug monitoring symposium recommended that research into factors affecting the decision making process in the assessment of benefits, risks and policy should be carried out.

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APPENDIX5F

INFORMATION PROVISION BY DRUG INFORMATION CENTRES - BRITISH AND AMERICAN EXPERIENCE

Hospital pharmacists have found that their role as traditional formulators and dispensers of medicines has been appropriated by the pharmaceutical industry. Manufacturers increasingly produce their drug products in unit doses and prepackaged format. As the pharmacist has lost control of the dispensing of medicines, medicines themselves have become increasingly more potent and complex. Consequently, the pharmacist has assumed a new role,

> "to assist in efficient prescribing by advising upon the nature and properties of medicaments and upon the selection of the most suitable substances and the form in which they should be prescribed." 1

The Working Party[1] also states that although the eventual scope of this advisory role cannot be precisely determined, the following functions are generally accepted at present:

1. drug formulation, stability, incompatabilities and conditions of storage;
2. dosage and methods of administration;
3. qualitative and quantitative identification of drugs and pharmaceutical preparations;
4. drug interactions, contraindications and side effects;
5. drug costs and sources of supply;
6. co-operation with clinicians in the provision of a drug information service.

In order to co-ordinate the provision of drug information on the numerous compounds and the large volume of explanatory

material from both professional journals and commercial sources, the information services offered by pharmacists were formalised by establishing drug information centres. The first centre was established in the U.S. in 1962, at the University of Kentucky. The need for such a service was summarised by Franke,

> "...the growth and complexity of the drug literature calls for the establishment of a Drug Information Centre as a unit of the pharmacy department with a well trained and highly motivated pharmacist in charge. This would provide a centralised unit from which the medical and allied staffs could obtain comprehensive pharmaceutical and drug information related to patient care, teaching and research... There is not the need so much for more drug information sources as there is for the organisation and centralisation of information now available and for an experienced and well qualified person to disseminate it." 2

The director of the then newly established centre stated that

> "The purpose of this Drug Information Centre was to organise and make available to all professional staffs drug information which would be useful in promoting a more rational drug therapy, to facilitate the teaching programmes of the colleges of medicine, dentistry and nursing and to study the patterns of drug utilisation for patients treated at the medical centre." 3

Since then, at least 74 organised drug information centres have been created in the U.S.[4]

Services in the U.K. were first introduced in 1970, at the London Hospital and Leeds General Infirmary. Rogers and Barrett[5] stated that the centre at the London Hospital was established to meet the demand for information, particularly from medical staff, within the hospital. The centre at Leeds became the first regional centre in 1973. Drug information services in the U.K. are organised by a regional or central information unit providing support for smaller area or hospital

based services. Eleven regions in England, three in Scotland and one in both Northern Ireland and Wales have established centres at regional level, most of these serving area information units. Some regions rely only on a network of area units. The overall objective is

> "to provide advisory information to medical and allied staff in hospitals and in the community to achieve maximum safety, efficacy and economy in drug use." 6

In 1975, the Regional Drug Information Pharmacists Group was established to promote co-ordination between the centres and to avoid duplication of effort.[7]

Service Provided by British Drug Information Centres

The major part of the service involves answering enquiries. Questions asked have been divided into two groups - those requiring opinion e.g. pharmaceutical,clinical etc. and those requiring factual data. For any opinion other than pharmaceutical, experts in the appropriate fields are contacted. For factual data, (if detailed searching is required) the assistance of librarians and information systems are sought.

Many centres actively provide information by producing and disseminating current awareness bulletins, usually on topics of local interest. Other centres supply abstracts of articles particularly to inform the prescriber of potential hazards recently reported and of new products available.[8] Other functions of centres include collecting data on adverse reactions and drug interactions and lecturing to members of the health professions.[7]

Service Provided by U.S. Drug Information Centres

There is no overall national organisation of centres in the U.S. although several statewide centres have been established. Rosenberg et al[4] list the location and description of the 74 U.S. drug information centres which accept drug information requests on a regular basis from health-care professionals. Analysis of these data shows that 88% of the centres provide "programmed" education - newsletters, columns, lectures etc.; 97% offer educational programmes for pharmacy (and in one case, medical) students; 39% provide drug abuse information and 38% serve as a major poisons information centres. Only one centre charged individual enquirers for use of the service.

Use of British Drug Information Centres

Leach[6] and McCabe et al[9] analysed the types and sources of enquiries made to eight regional centres in the U.K. and one in Scotland, respectively. All data quoted referred to 1976, but the Scottish report referred to only part of this year. The results are shown in Table 1 (see page 233).

The majority of enquiries were received from hospital doctors and hospital pharmacists, in both the studies.

The most common type of enquiry received by the U.K. centre concerned drug treatment, indications, dose, route and precautions, and by the Scottish centre concerned indications and dosage.

The average number of enquiries made per week to the eight British centres was 20.6 (standard deviation 12.6, range 7.9 - 37.8). Lawday[10] pointed out that the total number of enquiries received by regional drug information centres represented only a small percentage of the enquiries made annually to all

TABLE 1

TYPE AND SOURCE OF ENQUIRY RECEIVED BY EIGHT REGIONAL DRUG INFORMATION CENTRES IN THE U.K. AND ONE IN SCOTLAND DURING 1976

Enquiries	U.K. centres *	Scottish centre ‡
Total Number of Enquiries	8584	311
Type of Enquiry	% of total	% of total
Adverse effects	18	21
Availability, synonym, identification	19	..
Drug treatment, indications, dose route, precautions	36	..
Pharmaceutical and other	27	..
Availability	..	18
Indications and dose	..	27
Interactions	..	9
Cost	..	2
Pharmacokinetics	..	2
Pharmaceutical aspects	..	6
Other	..	16
Source of Enquiry		
Hospital practitioners (total)	41	40
Consultants	(11)	..
Junior doctors	(29)	..
General Practitioners	2	1
Hospital pharmacists	34	47
Nurses	11	5
Retail pharmacists	4	3
Other	8	4

* Source: Leach[6]

‡ Source: McCabe et al[9]

Key .. denotes data not measured

information services in each region. It is not possible to state the frequency of enquiries made to the Scottish centre, because the exact period over which the data were collected was not specified.

Use of American Drug Information Centres

Rosenberg et al[4] tabulated the average number of enquiries received per month by drug information centres in the U.S. between 1973 and 1976. The data show an increase in the number of enquiries received during this period.

Data concerning the type and source of enquiry received by 55 centres are shown in Table 2 (see page 235). Unfortunately, it is not clear which type of enquiry is the most common, because the authors of the article stated that enquiries concerning therapeutic use were the most common, but a figure showed that a greater percentage of enquiries about dosage were received.

The average number of enquiries received per month by the 55 American centres was 234. Thirtyeight percent of the enquiries were considered to be of a judgemental nature. Grace and Wertheimer defined judgemental questions as those requiring

> "the integration of data or knowledge and experience in the process of making a decision regarding a specific therapeutic problem." 11

Comparison of the data obtained from the American and the two British studies was made with several reservations. Firstly, differences in the type of enquiry received may simply reflect different emphases in drug therapy in the two countries. Secondly, differences in the source of enquiries may be a result of different ratios of health care professionals in the two countries. Thirdly, since drug information centres in the U.S. have been in existence for longer than their British counterparts

TABLE 2

TYPE AND SOURCE OF ENQUIRY RECEIVED BY 55 DRUG INFORMATION CENTRES IN THE U.S. DURING 1976

Type of Enquiry	% of total Enquiries
Dosage	16
Therapeutic use	12
Identification	11
Adverse effects	9
Toxicity	8
Availability	8
Side effects	7
Pharmaceutical compatability	6
Drug interactions	4
Therapeutic compatability	4
Foreign drug identification	3
Contraindications	2
Metabolism	2
Others	8
Source of Enquiry	
Pharmacist	37
Physicians	25
Nurses	15
Others	23

Source: Rosenberg et al[4]

their role in medical care may be more firmly established. This may affect both the source and total number of enquiries received. Fourthly, the data themselves were a limiting factor, because the reported categories of enquiries were all subject to interpretation by both the information staff providing the data and the authors of the articles.

Despite these reservations, the main difference was the greater percentage of enquiries received from doctors, by the British centres. In addition to the reasons stated above, this may be due to 11% of the American centres not being affiliated to either a hospital or a medical centre, whereas all the British centres are fully integrated into the hospital environment.

American drug information centres received a lower percentage of enquiries concerning adverse effects than British centres. The reason for this may be related to the recent "practolol disaster" that occurred in the U.K. (The therapeutic disasters associated with thalidomide and practolol did not occur in the U.S. because the Food and Drug Administration took seriously the first reports of side effects due to thalidomide, and refused to clear practolol for marketing because it represented no therapeutic advance on another product, propranolol, which had a similar type of biological activity.) However, a recent study reported that a sample of American patients suffered more adverse reactions than a comparable sample of Scottish patients.[12]

One American regional drug information centre reported receiving 95% of its enquiries between 07:20 and 18:50.[13] Approximately 50% of the calls were received before noon, and about half after noon.

Value of British Drug Information Centres

The value of British drug information centres has, to date, only been assessed in terms of the volume of enquiries received. The North-West Regional Drug Information Service received a steadily increasing number of enquiries between July 1974 and June 1977, and this presumably indicates its increasing value to health care.[6] The value of pharmacy-based drug information centres has been challenged by Rawlins and Davies who stated that

> "pharmacists have little training in clinical medicine, and therefore they are unable to offer expert advice on interactions between drugs and disease." 14

For this reason a group of eight clinical pharmacologists (all medically qualified) established a clinical drug information centre in the Northern region, with the aim of providing their medical colleagues with

> "clinical information and advice on all aspects of clinical pharmacology, clinical pharmacokinetics, therapeutics and toxicology." 15

After the centre's first year of experience, it was concluded that,

> "as most enquiries are consultative - that is requiring a clinical opinion - they can be managed only by someone with a medical qualification, clinical training and special expertise in pharmacology."15

Davies et al[15] commented that drug information and advice would only have any impact if it was provided by specialised medical staff. 82.5% of the enquiries received in the first year of operation were made by medical personnel (including hospital doctors and general practitioners). The majority of enquiries received (78.4%) required clinical pharmacological advice.[16] However, as this centre only received an average of 8.7 enquiries per week, it has an even greater problem of

low usage than the pharmacy-based drug information centres.

Not surprisingly, pharmacists seem to use pharmacy-manned centres and medical doctors tend to use clinical drug information centres. Mawer and Leach[17] suggested that active co-operation between clinical pharmacologists and drug information pharmacists would provide the most effective information service.

The pharmaceutical industry has also challenged the value of NHS drug information centres. The industry invests resources in information because of the need for internal information to research and market products. Staff and departments specialise in literature searching and information. Most companies recognise the need for a back-up service to be provided to the prescribing physician, to ensure the correct usage of their own products, and hence extend their services outside the company.[18] Drug information centres in the industry have access to all the detailed knowledge accumulated from the time the drug was first developed,[19] and many scan the world's literature using commercial sources or their own staff, storing references on well run data bases.[20] Thus information departments in the industry have the following advantages over their NHS counter-parts:

1. most industry information departments have their own budget in addition to access to journals taken by the company as a whole, whilst NHS centres were estimated to have a total annual budget of £500,000;[21]
2. information handled by industry centres is confined to their own products, and to a certain extent, competitors' products, whereas NHS centres keep information on all products used in their particular region;[22]

3. the industry is able to keep more up-to-date and comprehensive records of adverse effects occurring with the administration of their products. Although the same information about incidence of adverse reactions is ultimately available to both type of centres in the lists published by the Committee on Safety of Medicines (CSM), these publications appear infrequently. Many pharmaceutical firms, on notification of an adverse reaction, elicit information from the doctor who has informed them. The pharmaceutical industry is required by law to report all notifications to adverse reactions to the CSM.

Both the pharmacy and clinical drug information centres have the following advantages over information departments in the pharmaceutical industry:

1. the information pharmacist is not subjected to any commercial pressures whilst providing information. This does not necessarily mean that NHS centres provide unbiased information, because any information will be subject to personal bias in either the method of retrieval, or in its evaluation for use. Similarly, staff in information departments in the industry do not necessarily always provide commercially biased information;
2. drug information centres are easily accessible by medical staff and available on one telephone number. To contact a manufacturer is a slightly more time-consuming procedure. In addition, telephone calls to drug information centres are always local and therefore can be cheaper than calls to manufacturers;

3. information provided by drug information centres can be tailored to local needs;
4. co-ordination between centres allows a wealth of knowledge to be built up on specific topics (e.g. drugs excreted in breast milk[7]). It would be very difficult for manufacturers to collate this sort of information;
5. drug information centres can act as a focal point for receiving and disseminating information;
6. drug information centres can collect information on drug use in minority patient groups e.g. pregnant, geriatric and paediatric patients.

Value of American Drug Information Centres

Several studies have attempted to assess the value of American drug information centres. Rosenberg et al[4] reported an increase in the number of enquiries received by centres between 1973 and 1976. Smith et al[23] found that only 14% of a sample of 5,600 doctors had used a drug information service, although of those who had, 81% stated that it met their needs. Fifty percent of the sample felt that a drug information service would satisfy their needs more efficiently than sources currently being used. Thirtynine percent stated that they would be willing to pay for the service after an initial free experimental period. This result represents a conception of value which was not based on experience of use of the service.

Groth[24] surveyed users of a regional drug information centre and found that 81% of the respondents rated the overall quality of the information that they had received as high. Fiftytwo percent of the users indicated that the information

directly benefited patients, and 94% felt that, according to their own criterion, the information was received promptly. Only 59% indicated that they would have requested the information if there had been a charge for the service.

Pearson[13] asked users of the Michigan Regional Drug Information Network whether answers provided to a sample of enquiries were sufficient. 92.5% indicated that they were, but information concerning side effects, contra-indications, toxicity and metabolism was considered less satisfactory than answers provided to other questions.

Grace and Wertheimer[11] considered the number of judgemental enquiries received by a service to be indicative of its value. Only 4.6% of the questions received by one centre were judgemental and the reasons that were suggested for this included:

1. the need for drug information centres has been replaced by the clinical pharmacist who attends ward rounds;
2. the number of new products being introduced is continually decreasing and therefore there is less confusion and less demand for a drug information service;
3. the number of specialist physicians is continually increasing, and since they use a smaller range of products than general practitioners, they may be able to fulfill their own information needs.

Merritt et al[25] using Grace and Wertheimer's definition of judgemental questions reported receiving 28% of all enquiries in this category. The majority of these were classified as

"pharmaceutical" enquiries. Rosenberg et al[4] found that, 38% of the enquiries received by the average drug information centre were judgemental. These fairly large variations may be due to the difference in type of service offered by individual centres and also the interpretation of judgemental questions.

Rosenberg et al[4] stated that the majority of the 55 centres reported that users had often changed their drug therapy as a result of the answers provided. Unfortunately, this was a personal opinion of staff in 31 centres and hence not an objective assessment of value.

Halbert et al[26] presented 90 drug information centres with the same enquiry, in an attempt to assess comparative value. The enquiry concerned an overdosage with a foreign brand of tranquiliser. Eleven percent of the centres were unable to identify the product, although the information was easily traceable in several standard drug information textbooks. The caller provided a detailed account of the patient's condition and asked for advice. Only 53% took advantage of this opportunity to assist in the making of a therapeutic decision. Only 30% of the centres offered to provide a written follow-up of the information provided. However, since a request for a written answer may be unusual, the poor response to this request may be indicative of an unwillingness to provide more than an adequate answer. The authors assess the efficiency of the response in terms of the ratio of contact time to total call time. The average efficiency was 53%. Twentyfour percent of the centres were inefficient and conveyed wrong or incomplete information which was delivered hesitantly and uncertainly. Halbert et al conclude that drug information centres do fall

short of their objective to provide rapid, accurate and concise information. They also suggest that minimum standards should be defined.

This method of assessment is probably the most useful of all those reported, because it attempts to study the service in an objective manner. The majority of information staff in the 47% of centres that declined to offer advice about the overdosage treatment, stated that the physician would have to make the final decision. This implies that either the information pharmacist did not want to find out the necessary information, or he believed that pharmacists suggestions would not be considered seriously by the physician. Bell et al[27] discovered that 71% of the suggestions made by pharmacists were read, accepted and used by physicians.

A common feature of British and American drug information centres is that they are underused. The majority of the studies that assessed the value of centres to health care did not attempt to study the underlying cause for the low usage. Centres in the U.S. appear to have an additional problem of competition between the different types of centres (hospital, regional, statewide etc.).

It is apparent that both the clinical and pharmacy based drug information centres in the U.K. are of value and the formal amalgamation of both types (as has recently occurred in the Northern region[28]) offers the possibility of a vastly improved information resource. Kendall[29] recommends that clinical pharmacologists should avail themselves of the information service provided by the industry. An extension of this view is an improved liaison between information departments

in the industry and the combined clinical and pharmacy drug information centres. This liaison, to be successful, would require the scope and role of all types of centre to be precisely defined, to prevent overlap and resentment. One possible suggestion would be to allow the NHS centres to use the resources of the industry. In return, the centres could provide information to each firm on use of their products in unusual clinical situations, such as unauthorised indications and in minority patient groups.

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APPENDIX 5G

The ABPI Code of Practice for the Pharmaceutical Industry (fourth edition, 1974) states the following about the provision of information:

"Nature and availability of information

1. Upon reasonable request, the manufacturer shall promptly provide members of the medical profession with accurate and relevant information about the medical products which he markets.

2. Information about medical products should accurately reflect current knowledge or responsible opinion.

3. Information about medical products must be accurate, balanced and must not mislead either directly or by implication.

4. Information must be capable of substantiation, such substantiation being provided without delay at the request of members of the medical profession."

CONCLUSIONS

The communication of drug information must be efficient to promote rational, safe, effective and economic use of the ever increasing numbers of drugs. In this study, some of the major ways in which information about drugs is received and sought by hospital doctors have been examined.

The government currently controls the provision of drug information in three main ways. Firstly, it requires that each doctor is presented with an objective statement, in a standard format (the data sheet), which describes each marketed product. The exact requirements are laid down in the Medicines Act of 1968. Secondly, it requires that drug advertisements do not provide misleading information, and that only the uses which the government has approved can be recommended for products. Thirdly, it is reducing the promotional expenditure of the pharmaceutical industry by disallowing amounts in excess of 10% of sales to be included in the cost of drugs to the national health service. Although in the past the government has attempted to provide drug information, the Medicines Commission does not appear to be resuming an advisory role.

Sources of information that the prescribing doctor uses to learn about drugs do not provide all the information that he requires in a concise format. There seems to be a need for a regularly updated reference manual which provides this information and is easy to carry around. The data sheet compendium does not fall far short of these requirements, and would probably meet them if information about product efficacy,

possible drug interactions, cost and pharmacology (absorption, distribution and excretion of a drug) was added.

It was noted that the summaries of reports of clinical trials tended not to state the type of action that the trial drug had (e.g. anti-convulsant), the dosage schedule used by the trial subjects, the duration of therapy and the significance or lack of significance of the results. Since the majority of hospital doctors use reports of clinical trials to obtain information about new drugs, it appears that the addition of this information would make their search for information an easier task.

Although promotional material was found to provide little of the information that the prescribing doctor required, it was recognised that the majority of doctors only use this source to find out about the existence of a new drug. An improvement in the information provided is expected in the near future, when the Association of the British Pharmaceutical Industry's new code of practice is published and becomes operational. This together with the reduction in sales promotion expenditure could change pharmaceutical advertising, hopefully to include more prescribing information.

Two major issues were found to affect the provision of drug information by medical information staff in the pharmaceutical industry. Firstly, although the majority of the staff who were interviewed claimed that they did not provide biased information, it may be difficult for a doctor to accept this. Bias is a difficult concept to define, but since the salary of all information staff in the industry does depend on the commercial success of the firm that employs

them, it would be very difficult to avoid recommending the use of their own firms's products unless there was a specific reason for not doing so. It might be worthwhile reconsidering the role of medical information departments in the pharmaceutical industry in the light of recent developments. This leads on to the second issue affecting the provision of information by industry based departments. There appears to be some conflict between the role and aims of these departments and those of drug information centres set up in the national health service. This conflict is disturbing, because lack of co-operation between the two types of information service could result in the total duplication of information resources. However, there does appear to be a distinct role for an information specialist who retrieves drug information. This has resulted from the ever increasing volume of published literature which describes the ever increasing numbers of drugs, and therefore information retrieval for the doctor becomes a difficult and time consuming process.

Close co-operation between the two types of information service could provide an efficient information resource for the prescribing doctor. This co-operation could take the form of extending the use of the vast resources of the industry to the centres, who in return could collect detailed drug information about products in normal and unusual clinical situations.

In summary, it appears that the prescribing doctor requires an easily accessible reference manual, which contains drug information in a concise format. This could be backed up by a fully comprehensive drug information service which

has access to a large number of resources, and the expertise of drug information staff, and could be used to answer more detailed questions.

PROVISION AND USE OF DRUG INFORMATION

by Patricia L. Hibberd

ABSTRACT

There are numerous sources of information about drugs, but this does not necessarily mean that the information supplied by any particular source is adequate for the needs of the prescribing doctor. The government, the pharmaceutical industry, members of the health care professions and private business concerns have attempted to provide comprehensive information on drugs.

The ways in which the government has both provided and influenced the provision of drug information are described.

A survey was carried out to establish which sources of information are used by hospital doctors for prescribing and for learning about new drugs. The majority of hospital doctors use reports of clinical trials published in medical journals to learn about new drugs. A study of the information contained in a sample of trial reports appearing in several major medical journals is reported.

Many doctors indicated that promotional material was an important source of information, particularly for learning about the existence of a new drug. Several studies of the information provided by the various forms of pharmaceutical promotion have been made, and these are critically reviewed.

Finally, since the majority of hospital doctors had written to a pharmaceutical firm for further information about a drug, at some stage in their medical career, a survey was carried out to discover how medical information staff in the pharmaceutical industry provide information about drugs to the medical profession.

There appears to be a need for a regularly updated manual providing the information that doctors require in a concise format, backed up by a drug information service which would answer more detailed questions.