Information centres in the pharmaceutical industry— the prime source of drug information?

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Summary

The case is argued that the prime source of information is the manufacturing company. The medical information department of an average-sized company is used as a model to support this argument.

Introduction

The author supposes she was asked to talk on behalf of the industry because the company she works for has a medium-sized department and, like many other British groups, is a major subsidiary of a multinational company with interests in several major therapeutic areas.

Thus, the aims and resources of this company are reasonably representative of the industry as a whole. Its techniques are not highly sophisticated. However, an attempt will be made to demonstrate a little of the information the company is able to provide, in the hope that this will, in some way, answer the question posed by the organizers of this meeting.

First of all, it should be emphasized that the author is talking mainly about the industry's information resources for branded products, where information, particularly on new products, is continuously being updated and extended. Obviously, there are a number of products not manufactured by major research-based companies, of which those surviving, after the Product Licence of Right Review, should be covered by Martindale or textbooks of pharmacology and therapeutics, especially if they are a major resource in the medicinal armamentarium. Thus, the industry demonstrates an ability to provide the primary information resource on a reasonable proportion of the medicinal products in use—many of which are potent and provide the major therapeutic tools available to physicians today.

Why does the industry invest resources in information?

Information is an essential ingredient of research and development and of patenting. Similarly, clinical research is dependent on an interactive information flow. Thus, to research and to market a medicinal product is closely bound to a need for internal information, and it is this need which leads to the creation and staffing of departments special-

izing in literature searching and information. Most companies also recognize that the marketing of potent products with complex pharmacological activity requires a back-up service to the physician and for this reason information services are made available outside the company. A product can only be marketed successfully if its full potential, as well as its toxicity and side effects, are understood. So the information flow must be two-way, in order that a full *product profile* may be built up. The development of this detailed *product profile* is the crux of the author's whole argument for the value of industrially-based information resources, and this will be illustrated by reference to a product group manufactured by E. R. Squibb & Sons. The chosen compound is the potent phenothiazine, fluphenazine, and its long-acting esters, fluphenazine decanoate and enanthate. These esters were marketed 8 and 10 years ago respectively during the era of the Committee on Safety of Drugs when voluntary submissions were made by the company to the Dunlop Committee. The development of the care of patients with long-acting neuroleptics was pioneered and revolutionized through clinical research with these products, and this is deemed to illustrate very well the industrial ability to build a full *product profile*—which is still, of course, 10 years later under considerable development and improvement. The reason why information on a drug is sought, and who seeks this information, should be considered. The average medicinal/pharmaceutical enquiry may be quite complex, and the best answer is achieved by an interactive process of question and answer, thereby evaluating the essence of the enquiry and matching the available data to answer it. Other enquiries may be more difficult, requiring a detailed knowledge of the field involved. Apparently simple enquiries may indicate a lack of experience by the enquirer and therefore will need a greater degree of interaction, or even education. This is the heart of an information officer's job—the ability to convert raw data into usable information in response to a request. The specialization of a company into a restricted number of therapeutic areas gives the company information officer the unique

FIG. 1. Expert back-up available to information department.

opportunity to become an expert, not only on the products themselves and their administration, but also on the fields of their application. This expertise is not only gained passively through searching the literature, but it may be derived actively through research and trial.

Not only does the industry specialize in distinct therapeutic areas, but it also builds up an information network which will be illustrated by reference to the author's own company. This company, of course, carries out its own local literature searching, but the parent company also provides computerized data retrieval services. It is suggested that the literature monitoring be called the 'passive' part of the information work, although those involved in this hard task might dispute such a description.

The 'passive' literature monitoring gives a starting point to the information build-up. However, the indiscriminate collection of literature without evaluation is no better than using a computerized data retrieval service. Thus, the literature must be evaluated so that it may, in turn, make its contribution to the detail of the *product profile*. The literature may provide an idea for clinical research, or reported results may need confirmation or clarification—and so the search for information becomes 'dynamic'. In addition, the industry watches for drug interactions and side effects. The industry has been criticized for not giving a better indication of the incidence of side effects in product data sheets. This is difficult, but the author feels that the central monitoring of adverse reactions by the industry currently provides better information than the yellow adverse reactions reports of the Committee of Safety of Medicines. These reports cannot be interpreted easily, since there is no background on which to evaluate the relevance of the reports—even recorded deaths pose problems of relevance.

For example, between June 1964 and October 1971 six fatalities were reported during methotrexate therapy. The side effect noted for one patient was nausea and vomiting. From the scant data available in the reports, the cause of death could, more rationally, have been attributed to the disease under treatment, rather than the drug therapy. Also, reports of depressive reactions during fluphenazine medication are misleading, since there is ample evidence that depression is part of the disease symptomatology rather than an adverse reaction to therapy.

Returning to the information department, an information officer or, where applicable, a clinician is seen dealing with enquiries through the experience and knowledge gained from monitoring the literature, the drug-in-use and clinical research. Even more important is his immediate access to personnel whose special expertise is available to help with a particular problem. The groups shown in Fig. 1 are able to give expert back-up but, more importantly, they may also make very positive contributions, particularly in the early days of marketing a new drug, e.g. a clinical trial worker may be called upon to act as the outside expert and provide guidance in areas where clinical usage has been restricted. Physical compatibilities may be investigated by a quality control laboratory or a stability research group in response to a particular problem. Marketing personnel develop an expertise which may also contribute to the *product profile*. It should be remembered that a company representative first identified the interaction of monoamine oxidase inhibitors and cheese. Thus, returning to the structure of the author's own department (Fig. 1), which is fairly typical, this very considerable peripheral expertise may be called upon by the information officer, so that he is able to provide the specialized,

multidisciplinary service often required when dealing with specific product enquiries.

It should now be clear that the industry has a frank, commercial incentive to ensure the availability of adequate information resources since it is this incentive which provides the driving force to maintain the standards of information. It should also be clear that the requirement continuously to up-date and improve the product data, on a narrow front, should be exploited by those requiring information services, whether physician or information pharmacist. With almost 4000 drug entities, and in excess of 30 000 formulations available in 1976, it seems an impossible task to ask general information officers to achieve an equivalent expertise. They must know where to go, and how to elicit satisfactory information to answer an enquiry, and it is suggested that, in many cases, the industry has the resources and the expertise to provide this prime, evaluated product information.

Fear of commercial bias is the greatest criticism levelled against the industry providing product information. Advertising material does not in any way seek to act as the major source of information on prescribing, and it is obviously not ideal to have a marketing person preparing promotional platforms on one day and answering complex product enquiries on another. For this reason, the majority of companies have both pharmaceutical and medical advisers in order to provide the informational expertise necessary, and these advisers work within a separate medical department. If someone has developed a detailed knowledge of a product, he obviously thinks positively about it, but this does not preclude the provision of accurate information, e.g. a patient-orientated enquiry may necessitate the recommendation of a more suitable competitor. The provision of evaluated information by the industry is factual and, wherever possible, is backed by published evidence. However, the provision of every published paper in a particular field does not necessarily provide good evaluated information—only a complete bibliography, and in many instances presentation of key information is more helpful. Where opinion is the only possible guide-line, referral is frequently made to an expert.

Thus far, the *product profile* which is built up to meet the information needs of many groups, from prescribing physician to pathologist, from pharmacist to patient, has been discussed. A brief illustration of this is now put forward by reference to the information resources of the Squibb company for the fluphenazine esters.

Following a decade of clinical use, these products have made possible the control of chronic schizophrenia, allowing many patients to return to a useful role in the community. Clinical research was,

therefore, and still remains, a vital link in the acceptance and usage of these products. The Dunlop submission is the prime source of information and still holds, in unpublished form, useful data, e.g. studies on toxicology.

These data have been collated with extensive clinical experience and background from the world literature into Data Sheets, a technical booklet and patient cards as the first outward flow of information. It is intended that this type of company information, and not advertisements, be used as a basis for prescribing—all advertisements state that further information is available, on request, from the Technical Services Department. Since the technical booklet is a sound and detailed introduction to the use of both fluphenazine esters, it is intended that this should always remain available, and that it should be updated by an addendum; such an addendum is currently under preparation in order to highlight more recent clinical findings.

The 'passive' data collection from the world literature is, therefore, an essential back-up to the company's activities. These data are abstracted and retrieved from an edge-notched card system, and now represent well in excess of 1000 papers for the long-acting esters. These papers are classified into groupings relevant to the company's research and interests, and each group holds no more cards than can be searched easily at one time. Searching in this fashion may be slower than automated methods, but frequent usage of the cards helps to refresh the memory of the information officer, and also helps a new member of staff to learn the more minute product details as well as the scope of information available for each product. Apart from the indexing system, there are always available the Index Medicus, or the parent company's computerized retrieval system, or a Medline/Medlars search. Extensive literature searches may be sought for internal use or as back-up to research. Additionally, in those fields in which the company is recognized as having special expertise, e.g. schizophrenia and its treatment or antifungal chemotherapy, requests for searches come from very varied sources and may cover quite obscure aspects.

The build-up of background information is therefore achieved from the literature, and the significance and relevance of the literature is monitored actively by the personnel responsible for the product. Essential, ongoing monitoring is also maintained in other areas, e.g. drug interactions and adverse reactions. Adverse reaction data are actively sought and built into an abstract system for quick retrieval in an emergency. For greater coverage, this is currently being indexed with reference to adverse reactions from the world literature into a quick-scanning system which will give an overview of all

the reported reactions and their approximate incidence.

The data build-up influences areas of clinical research, and double-blind studies must be initiated to demonstrate efficacy and to compare each long acting ester with new competitors. Commercial success of these products is dependent on their being accepted by psychiatrists. This, in turn, is dependent on many factors of a much broader implication than a knowledge of the therapeutic ratio. For example, a 25 mg intramuscular dose may be sufficient for either ester to control a patient for 3 weeks, and serum estimations are very difficult owing to the minute concentrations of this potent drug. Thus, research towards improving the sensitivity of suitable assay techniques must be monitored in order to take advantage of improvements in technology.

Again, the impact of such medication on nursing care, and the social implications for discharged patients, must be investigated if these products are to be accepted and used for a number of patients. Methods of evaluating a drug's performance and clinical trial design must be considered, and so symposia are arranged to bring people together in discussion; such symposia may be drug-orientated or disease-orientated.

All of these facets demonstrate both the generation and the collection of data towards the *product profile*. This is converted into information in response to a particular request. Many of these requests are repeated frequently, and the information may be easily accessible and quickly obtained through reference files which have been established over the years. Once the frequent need for such information has been identified, the background can be used to update the Data Sheet or the addendum to the technical booklet—a further very good reason for channelling information requests through the industry.

In addition to adverse reaction monitoring, special files, many of them with case reports, form a special monitoring of important aspects where controlled studies are impossible, e.g. use in pregnancy or long term side effects. The maintenance of these files, and the slow accumulation of this type of information is dependent on an information flow—and

here the industry can achieve a great deal, but it desperately needs the co-operation of prescribing physicians and information pharmacists. How often is the result of treatment promised effusively, but in the end nothing is forthcoming. A nine-month pregnancy is a long time but the chronic schizophrenic, in particular, remains under close supervision during her pregnancy.

Introspective building of a product profile is not enough. Interests must be broad enough to take in a knowledge of the field involved—psychiatry. This establishes contacts with experts and those with wide experience of the products in use. One's understanding should not be theoretical, it should be practical. Where one cannot hope to give adequate guidance, referral to an outside expert may be invaluable.

The *product profile* so carefully built brings together in one place, and with continuity, all the data available on the product concerned. The accumulation and evaluation of these data lead to *product knowledge*, and it is this specialized and detailed knowledge which forms the basis for a good information service.

It is acknowledged that the pharmaceutical industry's requirements have been a major impetus for the development of information science, and that the industry has both pioneered information techniques and invested large sums of money in information resources.

It is hoped that it is now evident that an industrial information officer, like any other information officer, can scan the world literature. However, by working in a narrow field he can also gain specialized and detailed knowledge. Perhaps most important of all, he has immediate access to other personnel whose expertise can be called upon with evaluation of the literature, and indeed can offer their own special skills, experience or advice. The industrial information officer has access to much unpublished data, and can, where appropriate, initiate research. The author believes the resources of industry are peculiarly rich and dynamic through the expertise represented by Fig. 1, and poses the question: Should these resources be tapped routinely, or can one afford to replicate them—partially or totally—in many centres up and down the country?