Middle Articles

CONTEMPORARY THEMES

Non-proprietary Names

VALERIE J. WEBB,* B.Sc., A.R.I.C.

Brit. med. J., 1968, 2, 484-486

The publication of the Report of the Committee of Inquiry into the Relationship of the Pharmaceutical Industry with the National Health Service 1965-1967 (the Sainsbury Report) has aroused considerable controversy over the relative merits of proprietary names and non-proprietary names. Unfortunately the term "approved names" appears to have been used in the report to represent non-proprietary names in general and not in the more specific way in which it has come to be applied in this country. Since publication of the report, correspondence appearing in the pharmaceutical press has made it apparent that there exists a great deal of misconception regarding drug nomenclature. The time would now, therefore, seem appropriate to clarify the meaning of the term "approved name," and to describe the mechanism by which non-proprietary names for medicinal substances are established both in this country and abroad.

Four Categories

There are basically four categories of designations for drugs. For chemical compounds the *systematic chemical name* is usually the first to be applied, but though this has the advantage of conveying the precise structure of the compound it is normally too unwieldy to be of any practical use. This leads to the coining of a *trivial name*, which will probably have considerable mnemonic value, but which will give little, if any, indication of the structure or the action of the drug. An example of this is thebaco, the trivial name for 7,8-dihydro-codeinone enol acetate, which has now been adopted as the official non-proprietary name simply because of established usage, international recognition, and the undesirability of introducing a second name for the same compound.

The *proprietary name* applied to a drug is usually registered by the manufacturer as a trade mark, and consequently becomes the exclusive property of that manufacturer, identifying his particular brand of the compound. In some cases the proprietary name refers not to the compound itself but to a formulation containing that compound. Since each manufacturer enjoys the privilege of being able to choose his own proprietary name, confusion is likely to arise when several different names are in use for the same compound. Hence the need for *non-proprietary names*, which are not subject to any proprietary trade mark rights and are therefore entirely in the public domain. They are sometimes referred to as "generic names," but this is a misnomer, since the term refers to a genus or class of compounds, an example being "barbiturate."

In some countries existing bodies, such as the French Pharmacopoeia Commission and the Nordic Pharmacopoeia Council, have assumed the responsibility of establishing non-proprietary names, whereas in other countries committees have

been set up specifically for this purpose—for example, the United States Adopted Names Council of the American Medical Association. In this country non-proprietary names are issued by the General Medical Council, acting on the advice of the British Pharmacopoeia Commission, which receives recommendations from its Nomenclature Committee.

British Pharmacopoeia Commission

The work of the British Pharmacopoeia Commission in the field of non-proprietary nomenclature began in 1939, when it was agreed that the Commission should co-operate with the Medical Research Council and the Association of British Chemical Manufacturers in devising names for British products that were to be introduced in place of foreign proprietaries and subsequently to be described in the *British Pharmacopoeia*. The intention was that the non-proprietary name assigned to a drug should become its pharmacopoeial title. In this way the names of the British products would be brought to the attention of the medical profession and fixed in the minds of the prescribers, so that should foreign drugs again find their way on to the British market they would be in competition with the British equivalents firmly established under well-known names. Thus 1940 saw the issue of the first list of non-proprietary names in this country, and they were referred to as British equivalent names. Later in that year it was agreed that the Commission should issue non-proprietary names for drugs even if there were no immediate intention to include their monographs in the *Pharmacopoeia*, and in May 1941 the first list of approved names was published.

The term "approved name" was used to indicate that a name had been recommended by the Commission and approved by the General Medical Council, and it still carries the same implication today. Approved names are assigned almost exclusively to pure compounds and not to mixtures or formulated preparations; hence the term has a far more restricted application than that indicated in the Sainsbury Report.

Guiding Principles

The chief considerations in the establishment of a non-proprietary name are that it should be easy to pronounce and remember, and, if possible, informative to the users—that is, to the pharmaceutical and medical professions. To achieve this end general principles were drawn up for guidance in selecting approved names, and these have been amended and augmented from 1940 up to the present time.

The original guiding principles stated that approved names should "(i) be free from any anatomical, physiological, pathological or therapeutic suggestion, and should not suggest the name of any disease or symptom; (ii) contain the salient syllables of the scientific chemical name; (iii) be of two, or

* Scientific Assistant to the British Pharmacopoeia Commission, London W.1.

at most four, syllables, and preferably include an indication of the potent element or constituent of the drug; (iv) be distinctive in sound and spelling; and (v) avoid the addition of a terminal capital letter." By 1958 principles (i), (ii), and (v) had remained essentially unchanged; principle (iii) had been modified to state that names should not, in general, exceed four syllables; principle (iv) had been expanded to say that names should not be liable to confusion with names already in use, and three additional principles were listed. These were: (a) that international non-proprietary names and names used in the *United States Pharmacopoeia* or in *New and Nonofficial Drugs* should receive preferential consideration; (b) that salts or esters should be named in terms of the substances from which they are formed to indicate the other components present; and (c) that cognizance should be taken of the names of closely related substances, and, where desirable, the name should show this relationship. Also the use of the following affixes was recommended in naming the classes of compounds indicated:

- ine for alkaloids and organic bases.
- ol for alcohols and phenols (OH group).
- al for aldehydes.
- one for ketones and other substances containing a CO group.
- barbitone or -itone for barbiturates.
- caine or -aine for local anaesthetics.
- sulpha- for sulphonamides (sulphanilamido compounds).

During the past 10 years these guiding principles have been influenced by those of other countries, with the result that those in use at the present time lead to the adoption of approved names that are, on the whole, more informative than those adopted earlier. The French Pharmacopoeia Commission strongly recommends the use of syllables that indicate the pharmacological grouping but that avoid therapeutic suggestion, and some such syllables have now been incorporated in our own guiding principles. For example, "gly" is used to represent oral hypoglycaemic substances, "gest" for progestational steroids, and "moxin" for monoamine oxidase inhibitors. However, whereas the French Pharmacopoeia Commission and most other national agencies rigidly use these affixes whenever they are indicated, our own principles state simply that if certain syllables are used they should be restricted to the corresponding groups.

Our current guiding principles state that:

- (1) An attempt should first be made to form a name including letters or syllables from the scientific chemical name. (In Great Britain this latter name should comply with the rules of nomenclature laid down by the International Union of Pure and Applied Chemistry as interpreted by the Chemical Society.)
- (2) For a chemically undefined substance an attempt should be made to form a name descriptive of its derivation or source. (This is exemplified by some of the antibiotics, such as spectinomycin, which is produced by the organism *Streptomyces spectabilis*.)
- (3) Names should normally be free from any anatomical, pathological, pharmacological, or physiological suggestion or therapeutic indication.
- (4) Cognizance should be taken of the names of closely related substances, and, where desirable, the name should show this relationship. (For example, diazepam, nitrazepam, and oxazepam are closely related derivatives of 5-phenyl-1,4-benzodiazepin-2-one.)
- (5) Names that may be misleading in suggesting a relationship should be avoided.
- (6) Names should be as short as is convenient. (This wording permits the selection of names that contain more syllables than is desirable, but whose very lengths convey information that would be lost if brevity were the overruling criterion.)
- (7) Names should be distinctive in sound and spelling and should not be liable to confusion with existing names.
- (8) Names that are difficult to pronounce should be avoided. (This is very much a matter for conjecture, depending largely on personal idiosyncrasies, but generally speaking approved names are adopted only if they are considered euphonious by all the members of the Nomenclature Committee.)

(9) The use of an isolated letter or number should be avoided whenever possible. (Occasionally it becomes necessary to distinguish between different members of the same species, and these are designated by a terminal letter—for example, polymyxin B.)

(10) Non-proprietary names issued by the World Health Organization or adopted by a national authority should receive preferential consideration. (It is not always possible to adopt an established name, even though that name may be highly desirable. For example, the international non-proprietary name gestonorone was found to conflict with two trade marks registered in Great Britain for pharmaceutical products, and hence gestronol was adopted as the British approved name for the same compound.)

(11) The last guiding principle lists the syllables whose use is recommended to indicate certain groups.

Choosing Acceptable Names

The advantage of using recognized syllables to indicate membership of a particular group of compounds becomes obvious when one considers the case of the penicillins. Originally, names for derivatives of 6-aminopenicillanic acid were based on the suffix "-penicillin," which resulted in the adoption of polysyllabic names such as phenoxymethylpenicillin. It then became obvious that, following the same procedure, any derivatives of phenoxymethylpenicillin would necessarily be assigned a name in excess of nine syllables. So the practice was abandoned in favour of names based on the suffix "-cillin," and this has resulted in the adoption of highly satisfactory names such as adicillin, nafcillin, and hetacillin.

There are several uncharted rules that appear to have found favour with the British Pharmacopoeia Commission's Nomenclature Committee, such as the use of the suffix "-fylline" for theophylline derivatives (acepifylline, bamifylline), and the use of "-orphine" for derivatives of morphine (etorphine, nalorphine). This latter practice is particularly desirable in drawing attention to a potentially dangerous class of compounds. The suffix "-perol" or "-peridol" is useful in indicating the grouping 1-[3-(4-fluorobenzoyl)-propyl]piperidine, which gives rise to the neuroleptic effects of compounds such as clofluprol and droperidol.

If a name devised according to the above guiding principles is reasonably short and euphonious, and is not dangerously similar to any existing name, its freedom from conflict with current trade marks in the pharmaceutical and medicinal fields must be established with the co-operation of the Trade Marks Registry. The proposed approved name is then submitted to the corresponding agencies in other countries for comment and criticism, thus enabling an evaluation to be made of the acceptability of the name on the international level. Obviously it is desirable that the same name should be adopted in all countries, but occasionally this is found to be impracticable, usually owing to the existence of a conflicting trade mark in one or more of the territories. Also it is far more difficult to select a name that will be acceptable on the international level than one that will be acceptable in this country alone, since a name that is euphonious and pleasant to English ears may be difficult to pronounce or have undesirable associations in a non-English-speaking country.

If, after consultation with the manufacturer and with other national agencies, a proposed approved name is found to be acceptable, the Commission recommends its publication, and, with the authorization of the General Medical Council, the name appears in a Supplementary List of Approved Names. These lists are published every few months, and are reproduced in the pharmaceutical and medical press. They are eventually incorporated in the booklet *Approved Names*, which is revised approximately biennially. The current edition of the booklet was published in November 1966 and contains over 1,000 approved names arranged alphabetically, together with their chemical names and any other names by which they are com-

monly known. It also contains an alphabetical list of about 1,300 "other names" with references to the corresponding approved names. The guiding principles appear in the introduction, and at the end of the booklet is a list of recommended names for commonly occurring radicals and groups. These trivial names simply provide a convenient way of writing the name of the inactive part of a molecule. For example, the tranquillizer prochlorperazine is marketed as three different salts—the dimaleate, the methanesulphonate, and the ethane 1,2-disulphonate. Now maleic acid is itself a trivial name, and to refer to an ester as a dimaleate is quite convenient, but if the chemical names are used for the other two acid radicals the names become unwieldy. Hence the compounds are referred to as prochlorperazine mesylate and prochlorperazine edisylate respectively. Other frequently occurring trivial names appearing in the list are "tosylate" for toluene-*p*-sulphonate, "embonate" for 4,4'-methylenedi-(3-hydroxy-2-naphthoate), and "napsylate" for naphthalene-2-sulphonate.

International Co-operation

The international aspect of non-proprietary nomenclature is dealt with under the auspices of the World Health Organization, to whom requests are made by the national agencies for the selection of nationally accepted names as international non-proprietary names (I.N.N.). In countries where no official body exists to deal with the selection of non-proprietary names a manufacturer may submit a name direct to the W.H.O. or, in some cases, through a national agency in a country where the drug is likely to be marketed.

The first meeting of the W.H.O. Subcommittee on Non-proprietary Names took place in 1950, when it was recommended that guiding principles similar to, but more comprehensive and consequently more restricting than, those in use in this country should be adopted. The subcommittee has met annually since that time, and has recently achieved the status of a full committee. Over 2,500 requests for international non-proprietary names have been considered in the last 18 years, and each year a list of proposed international non-proprietary

names has been published in the *WHO Chronicle*. At the time of publication of each list a statement is made to the effect that any interested party may file a formal objection to any of the names within four months of the date of publication. Such an objection is usually based on the existence of a conflicting trade mark in a particular territory, and precludes the use of the I.N.N. in that territory. In the absence of any objection to a name in the given period of time it is published in the *WHO Chronicle* as a recommended I.N.N. An I.N.N. to which an objection has been raised can never achieve the status of a recommended I.N.N. so long as that objection remains sustained, but only under exceptional circumstances is a name ever withdrawn from a list of proposed International Non-proprietary Names.

The guiding principles recommended by the World Health Organization are similar to our own, but in order to produce names that are acceptable internationally there is an added proviso that syllables such as "methylhydro" and "chlor" should be abbreviated—that is, to "medro" and "clo," etc.—and that, to facilitate translation and pronunciation, "f" should preferably be used instead of "ph," "t" instead of "th," and "e" instead of "ae" or "oe."

The measure of international co-operation that has been achieved in the field of non-proprietary nomenclature is worthy of note, and any action that might disturb the harmonious relationship existing between the participating countries would be a matter for regret. It is possible that the suggestion in the Sainsbury Report that some of the principles, which have been so laboriously drawn up, should be abandoned could have just this effect. The experts faced with the responsibility of establishing approved names are already performing an unenviable task, and a situation where names complying with international principles would be unacceptable in this country could only succeed in making their job even more difficult. More regrettable, however, is the fact that such action would lead to a greater multiplicity of names, which is the very situation that non-proprietary names have attempted to avoid.

I wish to thank the British Pharmacopoeia Commission for permission to publish this article.

CONFERENCES AND MEETINGS

Psychiatry in Drug Dependence

The role of psychiatry in relation to drug dependence was the subject for discussion at a conference of the Psychological Medicine Group of the B.M.A. on 9 May.* Professor W. LINFORD REES (St. Bartholomew's Hospital, London) was in the chair.

The opening speakers were Dr. P. H. CONNELL, director of the drug dependence clinical research and treatment unit, the Maudsley Hospital, and a member of the Advisory Committee on Drug Dependence and of its Hallucinogens Subcommittee; and Dr. M. M. GLATT, director of the alcoholism addiction unit, St. Bernard's Hospital, Southall, and a member of the W.H.O. Expert Advisory Panel on Drug Dependence and hon. editor of the *British Journal of Addiction*.

Present Position

Dr. Connell dealt with the situation in relation to drug-taking in Britain in terms of the thinking behind recent developments, and

looked briefly at possible dangers which might have to be faced in the future.

Having outlined the rationale of the new approach, which included prescribing heroin to addicts who did not wish to be withdrawn from the drug, he drew attention to the diagnostic problem confronting the physicians working in the special centres which would deal with the treatment of heroin dependence. The physician wished to establish a number of facts, including whether the patient was taking heroin at all, if he was taking it what was the dose, whether he was taking other drugs, and whether he was taking it continuously or sporadically. When he turned to his colleagues in the fields of chemical pathology, biochemistry, and pharmacology he found to his dismay that quantitative assessments were not possible in an outpatient setting, and that qualitative methods, such as the use of thin-layer chromatography, could not be done quickly. He had there-

* A report of the business meeting of the Psychological Medicine Group is printed in the *Supplement* at page 147.

fore to try to play a waiting game, in which he attempted to gain the co-operation of his probably hostile and suspicious patient in an attempt to bring him back when urine test results were available. In the meantime he had to try to keep the patient going by giving a drug such as methadone to prevent possible withdrawal symptoms, should the patient actually be taking heroin. That was an unenviable state of affairs. The physician in the special centre had to face the fact that if he put too many requirements on the addict, such as daily attendance, spending an hour each time he attended and so on, the addict might become dissatisfied and seek a black market even though the drug was costly. Should enough addicts feel that way, a black market would be worth the while of the criminal organizations.

Thus, mainly for medico-social reasons, physicians had agreed to take part in a treatment setting which included maintaining a heroin addict on heroin, which was a very bad drug for maintenance purposes because of its short-lived action. The diagnostic