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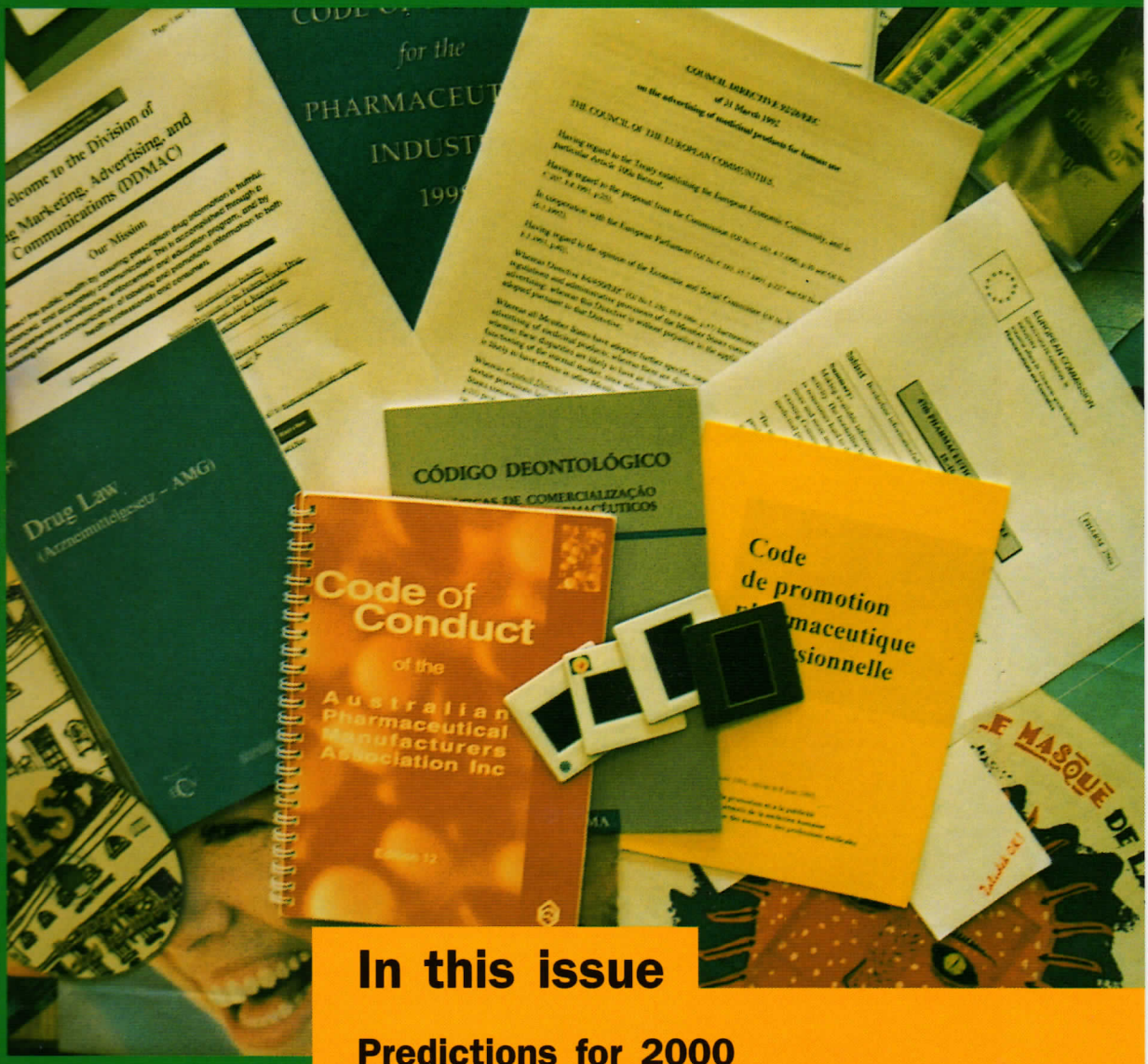

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Marketing medicines

A lack of harmonisation in the controls on prescription product promotion – can this continue?

PART I

"The promotion of prescription medicines to healthcare (H/C) professionals is a vital extension of the process of searching for and developing new and better means of preventing and treating illness

"As part of its commitment to health, the industry has an obligation and responsibility to provide accurate information and education...in order to establish a clear understanding of the appropriate use of prescription medicines

"Promotional activities (marketing practices) must be consistent with high ethical standards and information should be designed to help H/C providers improve services to patients. Information must be provided with objectivity, truthfulness and in good taste and must conform to all relevant laws and regulations. Claims for therapeutic indications and conditions of use must be based on valid scientific evidence and include clear statements with respect to side-effects, contra-indications, and precautions."

Extracts taken from the Code of Practice of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA)

The above extracts perhaps sum up reasonably succinctly why pharmaceutical product promotion is important to the industry, the healthcare professional and ultimately the patient, particularly in the context of the toxic nature of drug products if treated inappropriately.

In a previous article in this journal, the development of codes of practice and regulatory controls on the promotion of prescription drugs (Massam, 1999) was discussed.

In this article, in two parts, differences in the manner in which the promotion of prescription drug products are controlled internationally are reviewed. The arrival of the Internet, which knows no international boundaries, has highlighted these differences, and poses the question as to whether such differences are sustainable.

In Part I, the systems of control established in Europe will be briefly described and compared to those in other jurisdictions. In Part II, the status of Direct-to-Consumer advertising of prescription-only products. The use of the Internet for promotional purposes and the implications of the latter on existing controls in many jurisdictions are discussed.

Background

Most national regulatory authorities have enacted legislation to ensure appropriate pharmaceutical advertising and promotional practices. Additionally, industrial associations in many jurisdictions have instituted Codes of (Marketing) Practice, which set out standards of conduct for companies regarding promotion of prescription products to be used under medical supervision as permitted by their local legislation. Acceptance and observance of the Code is a condition of membership of the industrial association. The operation of these Codes are frequently supervised and administered by a Panel established by the association (self-regulation), supported in many cases by a further Appeal Board, and failure to comply results in sanctions. The Codes are frequently more detailed than the legislation, and in some cases include a requirement that a company's activities should not bring discredit upon, or reduce confidence in, the industry. All Codes of member associations of IFPMA embody the principles set out in the IFPMA Code, which was originally produced in 1981 in order to set out universal principles for IFPMA Code, which was originally produced in 1981 in order to set out universal principles for ethical marketing conduct, and to provide an operational Code to be used in countries other than those in which a more demanding Code already operates. (The current version is dated 1994 – it should be noted that some changes have since been made and came into operation in 1998). The European Federation of Pharmaceutical Industries and Associations (EFPIA) adopted its own code in 1991, and the current version dates from 1993 – individual member associations must adopt the Code or ensure their own national Codes fully reflect the standards of the Code in a manner compatible with national laws.

Scrutiny of a company's promotional activities may be carried out by competitors, industrial pharmaceutical associations, healthcare professionals, regulatory agencies, the press, and in certain circumstances, the general public. Where self-regulation applies, resolution of allegations of incorrect practice made by one company about another is normally expected to be initially attempted between the companies. In the absence of satisfactory resolution, and where allegations are brought by others, the complaints are handled by Codes of Practice Panels, where such exist, or the regulatory agency. Where no such systems exist, and the offending company is a member of IFPMA, complaints can be referred to this body.

European Union (EU)

The adoption and implementation by the member states (MS) of Directive 92/28/EEC of March 31, 1992 "on the advertising of medicinal products for human use" has brought a certain level of harmonisation into the control of prescription drug advertising. The Directive:

- Prohibits the advertising of prescription only products to the general public
- Prohibits the advertising of a product for which a marketing authorisation has not been granted
- States that all advertising must comply with the SmPC, shall encourage the rational use of the product, by presenting it objectively and without exaggerating its properties, and shall not be misleading.

However, since national legislation, guidelines and Codes of Marketing Practice, established by national industry associations were already in place prior to its development, the Directive is a basic minimum, as has been previously noted (Massam, 1999).

The Directive does not lay down any direction as to how MS should monitor promotional activities. Monitoring systems had previously been established in many MS, and in most cases, these were self-regulatory, established by the local national pharmaceutical industrial association, sometimes with the involvement of the Health Ministry.

In the UK, a Code of Practice was established by the Association of the British Pharmaceutical Industry, ABPI, in 1958 and may well have been the first such system introduced anywhere in the world (Massam, 1999). In 1993, the Prescription Medicines Code of Practice Authority (PMCPA) was set up as an independent body to continue the operation of the Code – the most recent version of which was published in 1998, although a further review is scheduled for 2000. Self-regulatory systems have also been established in Belgium (Code de Déontologie operated by the Industry association, l'Association Générale de l'Industrie du Médicament (AGIM)), Netherlands (Gedragscode geneesmiddelenreclame – NERFARMA), Denmark (Naevnet for Medicinsk Informations–materiale), Sweden (Regler fur Bedomning av Lakemedelsinformation – Lakemedelsindustri–foreningen), Ireland (Code of Marketing Practice (1999) – Irish Pharmaceutical Healthcare Association), and Portugal (Codico Déontologico – Associacao Portuguesa da Industria Farmaceutica (APIFARMA)).

In Germany, drugs advertising is regulated in the "Heilmittelwerbegesetz" (HWG, Law on Advertisements for medicines) and the "Gesetzgegen den unlauteren Wettbewerb" (UWG, Law against unfair competition). Compliance with this legislation is in principle carried out by the "Länderbehörden" (state authorities), not by BfArM. However, competitor companies and "Abmahnvereine" ("Integritas") – established by the BPI (Federal Union of the Pharmaceutical Industry) and BAH (Federal Association of Drug Manufacturers) – and the "Zentrale gegen den unlauteren Wettbewerb" (Office against Unfair Competition), mainly supported by the "Industrie und Handelskammern" (Chambers for industry and commerce) tend to be more active in this regard. The "Abmahnvereine" are empowered to take decisions, demand corrective action and impose fines. Recourse to the Courts is also possible. Codes of practice of the associations are available (eg, that of the BPI can be found at *http://www.bpi.de/kodex*) and comprise the relevant legislation and its interpretation, together with guidances – however, they are purely advisory.

Promotion of prescription products in Greece is expected to follow Directive 92/28/EEC, supplemented by a number of explanatory guidances issued by the National Drug Organisation (EOF). Monitoring, arbitration and handling of complaints are performed by EOF in the context of the Directive and the existing legislation.

Monitoring is conducted in Italy, France and Spain either by the Ministry of Health (MOH) or its appointed agency.

In Spain, the Industry association, Farmindustria, has produced a Code, which is essentially a translation of the EFPIA Code with some additions. Companies are required to submit their promotional materials to the local Health authority, Comunidad Autónoma de Madrid Consejeria de Salud (Madrid, or its equivalent in the other Comunidads), prior to use in the case of new products (during the first two years of marketing), or at the time of first dissemination in other cases. Prior approval is not necessary. At year end a listing of all materials used must also be supplied to the Authorities. Inter-company differences regarding promotional practices/activities are expected to be resolved *inter se*.

In France, l'Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSPS), through its "Unité de la Publicité et de Bon Usage du Médicament" is responsible for monitoring of medicinal product advertising. Advertising must be submitted within eight days of its initial use and is monitored *a posteriori*. The Unit's work is supported by "La Commission chargée du Contrôle de la Publicité et de la Diffusion de Recommandations sur le Bon Usage du Médicament", a consultative commission established by the MOH. The Commission issues recommendations on advertising and practices to the Director-General of the Agency, and may also issue recommendations on the correct usage of products. The industry association, Syndicat National de l'Industrie Pharmaceutique (SNIP) is currently working on the creation of a Code.

In contrast to all other MS, companies in Italy are required to submit to the MOH's Drug Evaluation Dept all promotional materials for approval prior to use. The material is considered approved if, after 45 days, no unfavourable comment has been received from the MOH. Permitted promotional practices are in general more limited as compared to other jurisdictions.

Most MS have controls in place through their Codes and/or national legislation which are far more restrictive than the Directive. In Italy for example, it is not permitted to promote using a product's brand name – the only occasion where this is possible being on the SmPC when this is distributed promotionally.

Further examples of differences in national policies include:

1. Acceptable data to justify promotional claims. In some jurisdictions, the use of "data on file" is accepted. "Data on file" constitutes unpublished data eg, new clinical trial data, but in France and Denmark, for example, the definition is limited to data that have been submitted to, and validated by, the national regulatory agency. Whatever the interpretation, the data must be consistent with the approved product labelling, and a company must be prepared to provide the supporting data upon request within a reasonable time period.

Other MS will not allow "data on file", but will allow reference to be made to an abstract of a presentation made at a respected international congress. However, this form of substantiation is not accepted in Spain and Denmark, and is only accepted in France for a period of one year from the date of the congress – the logic behind this being that the authority expects that valid data will be subsequently published. The preferred form of substantiation is by reference to a paper in a peer-reviewed scientific journal.

2. Medical samples. In principle, these may only be provided to healthcare professionals in response to written requests, and should be no larger than the smallest presentation on the market. In the UK and Spain, no more than ten samples of a particular medicine may be provided per professional per year, whereas in Ireland and certain Scandinavian countries, the permitted numbers are three and one respectively. In Belgium, the professional may not request more than 600 samples from all suppliers in one year.

3. Reminder ads/gifts/"gimmicks". In principle, such items should be inexpensive and relevant to the practice of the professional. Differences exist between MS on the interpretation of "inexpensive" and of their "relevance". In addition, whereas the approved prescribing information must be provided with all promotional materials, its application in respect of reminder advertisements varies. Most authorities consider that advertisements which do not include a claim about the product, but only act as a reminder of the brand name of the product, do not need to carry associated prescribing information. However, in France, even reminder ads must include such information.

Comparative advertising

Attitudes to comparative advertising differ across the EU. In some MS it has been permitted but in others it has either not been allowed (eg, Italy) or has been so circumscribed as to make it impractical (eg, possible in the Netherlands only if based on data from two independent comparative trials). However, after years of discussion, "Directive 97/55/EC of the European Parliament and of the Council of October 6, 1997 amending Directive 84/450/EEC concerning misleading advertising so as to include comparative advertising" was adopted in October 1997. It establishes the conditions under which it can be carried out, and must be implemented by member states by April 2000.

Elsewhere in Europe

Norway

A self-regulatory system operates, the Norwegian Medicines Control Authority having delegated responsibility for the handing of promotional issues to the Industry Association, the Legermiddelindustri–forreningen. The Association has produced marketing guidelines, "Retningslinjer i markedsföringen av legemidler", and operates an Arbitration Panel to resolve complaints arising from contraventions of the guidelines. Companies are required to submit copies of all promotional materials to the Association.

Switzerland

A Code for the Promotion and Advertising of Pharmaceutical products for Human Use to Healthcare Professionals, established by the Swiss Society of Chemical Industries (SSCI), incorporates the requirements of the IFPMA and EFPIA Codes as well as national legislation. As a self-regulatory system, complaints concerning possible infringements of the Code are made to the SSCI's Secretariat, which includes an independent H/C professional with duties not only to assess complaints and as far as possible resolve such issues, but also to conduct random checks of promotional measures and materials. A Supervisory Board deals with cases referred to it by the Secretariat, and is empowered to seek redress for promotional measures it considers violative, and in the absence of corrective action by the offending company, will report the issue to the health authority.

Beyond Europe

Australia

The Australian Pharmaceutical Manufacturers' Association Inc. operates a self-regulatory system based on compliance with its Code of Conduct. The administration of the Code is supervised by the Code of Conduct Subcommittee of the Association.

Canada

A self-regulatory system also operates in Canada. A Pharmaceutical Advertising Advisory Board (PAAB) has been established and includes representatives from, among others, the industry, healthcare, consumers, pharmacists and advertising associations. It is an independent review agency whose primary role is to ensure that advertising of prescription drugs is accurate, balanced and evidence-based. The PAAB Code of Advertising Acceptance sets out the standards for the advertising of pharmaceutical products to the healthcare professions. Promotional materials must be submitted for PAAB acceptance prior to distribution to health professionals, and written clearance is given. Complaints are initially treated by the PAAB's Commissioner, and if conciliation is not achieved, the issue is decided by a Review Panel.

New Zealand

A self-regulatory system is also operated in New Zealand by the Research Medicines Industry

Association (RMI). The objective of its Code is to define and ensure high standards of conduct for promotional practices and, through application of the Code, demonstrate that the industry acts ethically and responsibly. Administration of the Code is supervised by a Standing Committee, which receives and determines complaints, appeals being possible to an Appeals Committee.

South Africa

The Pharmaceutical Manufacturer's Association of South Africa issued in August 1998 a revised Code of Practice for the Marketing of Medicines, which now incorporates the principles of the Codes of the EFPIA, IFPMA, PMCPC (UK), Advertising Standards Authority, WHO Ethical Criteria for Medicinal Drug Promotion and the Gulf Code of Pharmaceutical Marketing Practices. As with most Codes, it reflects and goes well beyond the national legal requirements controlling the advertising of medicines. Complaints made under the Code about promotional materials or practices are considered by the Disciplinary Committee or the Special Disciplinary Committee, and, where required, the Association's Appeal Committee.

United States

In the United States, promotional activities are governed by the Food and Drug Cosmetic Act, Regulation 21 CFR 202. The controlling agency, within the Food and Drug Administration, is the Division of Drug Marketing, Advertising and Communication (DDMAC), whose mission is "to protect the public health by assuring prescription drug information is truthful, balanced, and accurately communicated". The Agency reviews all materials submitted to it, considers complaints received from competitor companies, healthcare professionals, FDA staff etc, and conducts media surveillance. All promotional materials must be submitted at time of dissemination. Generally, promotional materials do not have to be pre-approved, except for products approved under subpart H (the accelerated approval procedure). However, the agency strongly recommends that launch materials and Direct-to-Consumer (DTC) broadcast materials (see Part II) are submitted for pre-approval, although it is not required under the regulations.

When promotional activities are found to be in contravention of the rules, the agency writes to the offending company either an "Untitled Letter" (formerly known as a Notice of Violation (NOV) letter) for minor violations or a "Warning Letter" for serious or repeat violations. These letters are also posted on the DDMAC website (*http://www.fda.gov/cder/ddmac*) – a major concern for the industry at the present time is that it has no form of adequate redress by way of subsequent corrective postings on the Internet, if, following subsequent discussions with DDMAC, the latter's position is modified in favour of the company.

International congresses

Many national agencies throughout the world accept that congresses, organised by well-respected international organisations (eg, the World Congress of..., European Society of... etc) welcome large numbers of international participants. Thus promotion at these congresses is not limited to products/indications, which are approved by the host national regulatory authority.

This position is taken by many of the MS in the EU. A number require, however, that if a product or indication is being promoted, but is not locally approved, then that fact must be identified for the benefit of visitors from the host country. In Switzerland, it is additionally required that a listing is provided of those countries where the locally-unapproved product or indication is registered.

By contrast, however, all promotion at international congresses in France, Belgium and Italy must be conducted in accord with the local regulations and marketing authorisations.

In the United States, companies often operate a booth that is clearly separated into two, one section for the benefit of visitors from the host country and the other for international visitors. In the former, all promotion must be conducted in accord with the US regulations and marketing approvals. In the latter, information regarding products/indications, that are not FDA approved, can be provided but entry to the area must be restricted to healthcare professionals who are not licensed to practise in the US.

It can be seen that there are national differences in the way prescription product promotion is controlled, in the regulations followed, and indeed, in certain instances, in their interpretation. More fundamental is the difference in attitudes towards promotion to the general public, which is not permitted in most jurisdictions. However, it is permitted in both the USA and New Zealand.

In the second part of this article, Direct-to-Consumer Advertising (DTC), as it is called, will be reviewed. The arrival of the Internet, a medium that knows no national boundaries, has opened up new opportunities for DTC. However, its borderless nature also provides difficulties for the regulators in terms of ensuring compliance with national regulations. This, together with pressure (certainly in the Western world) for a greater freedom of information, is causing a rethink in attitudes to DTC particularly in Europe.

Dr Owen Lewellen
Aventis Pharma
Antony, France

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Reference

D. Massam (1999). The development of controls on the promotion of prescription medicines. *ESRA Rapporteur*, Vol. 6, N°4, 15-18.