

GUIDANCE ABOUT CLAUSE 3

On occasion pharmaceutical companies will have a legitimate need to tell health professionals and others about unlicensed medicines or indications. This guidance will help companies understand how that can be done without breaching the Code, but is not a substitute for a good understanding of the Code.

The guidance reflects the requirements of the 2016 Code and although it focuses on Clause 3, other clauses of the Code might also be relevant. Companies should always bear in mind that overall impression created by activities, materials etc.

Clause 3 prohibits the promotion of a medicine prior to the grant of its marketing authorization. It also requires that promotion must be in accordance with the marketing authorization and not be inconsistent with the summary of product characteristics (SPC).

The supplementary information to Clause 3 provides additional detail, including a clear statement that the legitimate exchange of medical and scientific information during the development of a medicine is not prohibited provided that this does not constitute promotion which is prohibited by Clause 3 or any other clause in the Code.

Clause 1.2 defines 'promotion' as 'any activity undertaken by a pharmaceutical company or with its authority which promotes the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines'. This is followed by a list of materials and activities that come within that definition and a number that do not.

Companies need to start by considering two aspects. Firstly, whether the activity itself is promotional and secondly the role of employees carrying out that activity.

The Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for administering the relevant UK law and gives strong support to the ABPI Code. It is consulted on any changes to the ABPI Code and its operation.

The PMCPA cannot approve any materials or activities, it can only give informal advice based on its interpretation of the Code. If a complaint were received about a matter upon which advice had been sought, it would be considered in the usual way; the Code of Practice Appeal Board would make the final decision if a case went to appeal.

This paper focuses on Clause 3 but other clauses of the Code might also be relevant, including Clauses 7 and 9.10. Companies should always bear in mind the overall impression created by activities, materials etc.

1 PROVISION OF INFORMATION ABOUT UNAUTHORIZED MEDICINES/ INDICATIONS

In addition to the ABPI Code, the provision of information about unauthorized medicines/indications is covered by an EU Directive, UK law which is based on European law and the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code on the Promotion of Prescription Medicines to, and Interactions with, Healthcare Professionals.

EU Directive

The European Directive defines 'advertising' as:

'advertising of medicinal products' shall include any form of door-to-door information, canvassing activity or inducement designed to promote the prescription, supply, sale or consumption of medicinal products; it shall include in particular

- *the advertising of medicinal products to the general public,*
- *advertising of medicinal products to persons qualified to prescribe or supply them'*

The European Directive specifically excludes from the Directive and thus from the definition of advertising *'...correspondence, possibly accompanied by material of a non-promotional nature, needed to answer a specific question about a particular medicinal product'*.

UK Law

In UK law the term 'advertisement' is defined in The Human Medicines Regulations 2012 (Regulation 7). The exemption for correspondence is also referred to in Regulation 7.

ABPI Code of Practice for the Pharmaceutical Industry

Promotion prior to the grant of a marketing authorization is given as an example of an activity likely to be in breach of Clause 2 of the ABPI Code. This requires that activities or materials associated with promotion must never be such as to bring discredit upon or reduce confidence in the pharmaceutical industry. A ruling of a breach of Clause 2 is seen as a sign of particular censure.

The Code states in the supplementary information to Clause 3 that the legitimate exchange of medical and scientific information during the development of a medicine is not prohibited provided that any such information or activity does not constitute promotion which is prohibited under this or any other clause. In this regard the context in which the exchange takes place and the audience will be important factors in determining whether the activity is acceptable under the Code.

The proactive provision of information by a pharmaceutical company about the unauthorized use of a medicine (including 'off-label prescribing', 'near-label prescribing' or similar) is very likely to be seen as promotion and in breach of the Code. There are certain exemptions set out in the supplementary information and these are referred to below.

The UK law exemption to the definition of advertising *'...correspondence, which may be accompanied by material of a non-promotional nature, answering a specific question about a medicinal product'* is expanded in Clause 1.2 of the Code. This clause states that the term promotion does not include, *inter alia*, 'replies made in response to individual enquiries from members of the health professions or other relevant decision makers or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they relate solely to the subject matter of the letter or enquiry, are accurate and do not mislead and are not promotional in nature'.

The supplementary information to Clause 1.2, Replies Intended for Use in Response to Individual Enquiries, gives additional guidance as follows:

'The exemption for replies made in response to individual enquiries from members of the health professions or other relevant decision makers relates to unsolicited enquiries only. An unsolicited enquiry is one without any prompting from the company. In answering an unsolicited enquiry a company can offer to provide further information. If the enquirer subsequently requests additional information this can be provided and would be exempt from the Code provided the additional information met the requirements of the exemption. A solicited enquiry would be one where a company invites a person to make a request. For example, material offering further information to readers would be soliciting a request for that information. Placing documents on exhibition stands amounts to an invitation to take them. Neither can take the benefit of this exemption.

Replies intended for use in response to enquiries which are received on a regular basis may be drafted in advance provided that they are used only when they directly and solely relate to the particular enquiry. Documents must not have the appearance of promotional material.'

The reason for the exemption in the Code is to allow pharmaceutical companies to answer specific questions from health professionals and other relevant decision makers. One area that frequently comes up in this context is questions about unauthorized medicines or unauthorized indications. To ensure that the exemption was only used in relation to genuine enquiries the word 'unsolicited' was used. This was to clearly separate the promotion of medicines from the role of medical information departments. This section of the Code relates to interactions with health professionals and other relevant decision makers rather than to responding to enquiries from patients, the public or journalists which is covered in Clause 26 (see section 6 below).

Supplementary information to Clause 1.2 further states that price lists of unlicensed medicines which include no product claims and make clear that the products are unlicensed can be sent to health professionals and other relevant decision makers at reasonable intervals or in response to enquiries. They must not be used proactively in a manner which could be seen to be promoting unlicensed medicines, such as by displaying them on exhibition stands.

2 PROMOTION AT INTERNATIONAL MEETINGS HELD IN THE UK

The supplementary information to Clause 3 states that the promotion of medicines at international meetings held in the UK may on occasion pose certain problems with regard to medicines or indications for medicines which do not have a marketing authorization in the UK although they are so authorized in another major industrialised country.

The international meetings referred to in this supplementary information are those organised and run by learned societies not those organised by pharmaceutical companies and attended by health professionals.

The display and provision of promotional material for such medicines is permitted at international meetings in the UK provided that the following conditions are met:

- the meeting must be a truly international meeting of high scientific standing with a significant proportion of the attendees from countries outside the UK in which the product is licensed
 - the medicine or indication must be relevant and proportional to the purpose of the meeting
 - promotional material for a medicine or indication that does not have a UK marketing authorization must be clearly and prominently labelled to that effect
 - in relation to an unlicensed indication, UK approved prescribing information must be readily available for a medicine authorized in the UK even though it will not refer to the unlicensed indication
 - the names must be given of countries in which the medicine or indication is authorized which must include at least one major developed country and it must be stated that registration conditions differ from country to country
 - the material is certified in accordance with Clause 14, except that the signatories need certify only that in their belief the material is a fair and truthful presentation of the facts about the medicine.
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3 ADVANCE NOTIFICATION OF NEW PRODUCTS OR PRODUCT CHANGES WHICH MAY SIGNIFICANTLY AFFECT EXPENDITURE

The supplementary information to Clause 3.1, Advance Notification of New Products or Product Changes which May Significantly Affect Expenditure, describes certain, limited, activities that can take place prior to the grant of a marketing authorization in order to assist the NHS with financial planning. The supplementary information states that NHS organisations and others involved in the purchase of medicines need to estimate their likely budgets in advance and there is a need for them to receive advance information about the introduction of new medicines, or changes to existing medicines, which may significantly affect their level of expenditure during future years.

Companies can only provide advance notification if their new product or product change will mean that NHS organisations and others will spend significantly more or less to treat patients. When this information is required, the medicines concerned (or the changes to them) will not be the subject of marketing authorizations (though applications will often have been made) and it would thus be contrary to the Code for them to be promoted. Companies wishing to provide advanced notification must ensure that information is also provided wherever possible for inclusion in national horizon scanning databases. Non-promotional information may, however, be provided as advance notification, but it must:

- i) relate to:
 - (a) a product which contains a new active substance, or
 - (b) a product which contains an active substance prepared in a new way, such as by the use of biotechnology, or
 - (c) a product which is to have a significant addition to the existing range of authorized indications, or
 - (d) a product which is to have a novel and innovative means of administration
- ii) only be directed to those responsible for making policy decisions on budgets and not those expected to prescribe
- iii) state whether or not a new medicine or a change to an existing medicine is the subject of a marketing authorization in the UK
- iv) state the likely cost or savings and budgetary implications which must be such that they will significantly change the organisation's likely expenditure
- v) be factual and be limited to that sufficient to provide an adequate but succinct account of the product's properties; other products should only be mentioned to put the new product into context in the therapeutic area concerned.

The information provided must not:

- i) be in the style of promotional material – product logos should be avoided but company logos may be used; the brand name of the product may be included in moderation but it should not be stylised or used to excess
- ii) include mock up drafts of either summaries of product characteristics or package leaflets.

If requested, further information may be supplied or a presentation made.

If the product or indication has a significant budgetary implication but any of the other conditions are not met, then the proactive provision of information about the unauthorized medicine or indication is likely to be seen as promotion in breach of Clause 3.

Whilst neither the promotion of an unlicensed medicine or indication at an international meeting held in the UK, nor the provision of pre-licence information in relation to a medicine or indication with a significant budgetary indication, are referred to in UK law, the MHRA does permit such activities as set out in its Blue Guide on Advertising and Promotion of Medicines in the UK.

4 GUIDANCE ISSUED FOLLOWING HEALTH TECHNOLOGY ASSESSMENTS

On occasion guidance issued by bodies such as the National Institute for Health and Care Excellence (NICE), the All Wales Medicines Strategy Group (AWMSG) and the Scottish Medicines Consortium (SMC) is inconsistent with a medicine's summary of product characteristics. If the recommendation is for use outside the marketing authorization then this cannot be promoted by pharmaceutical companies. Drawing attention to such guidance in company materials or by representatives etc may be in breach of Clause 3.2.

5 PHARMACEUTICAL COMPANY STAFF

Another aspect to be considered is the role of various pharmaceutical company staff, particularly those in the field who call upon health professionals and other relevant decision makers to provide scientific and medical information. These staff have various job titles throughout the industry including medical scientific liaison, health economic adviser etc. Documentation (such as job descriptions, key skills, objectives, etc) and training are particularly important in clearly setting out the role.

It is not possible to set out the roles in detail as these vary from company to company. A general description of the role might be 'to provide a means of exchanging medical and scientific or economic information with healthcare experts'. Such roles could include responding to unsolicited, specific, individual requests for information from health professionals and/or other relevant decision makers, exchange of medical and scientific information during the development of a medicine, following up adverse drug reaction reports, identifying investigators for clinical trials, information gathering from certain groups such as key opinion leaders, budget holders etc, responding to enquiries from health professionals wishing to run their own studies, providing more detailed information on licensed products and licensed indications than representatives, responding to requests for more information in relation to budgetary implications of the introduction of new products or new indications for existing products, training company staff and providing disease area information, etc.

It is important to consider all the arrangements, whether the activities are compatible with each other if they are undertaken by one individual, and how the activities are perceived. The more functions combined into one role the more difficult it is to ensure compliance with the Code. In the event of a complaint each case would be judged on its own merits.

The Code defines a representative in Clause 1.7 as a representative calling upon members of the health professions and other relevant decision makers in relation to the promotion of medicines. This is a wide definition and can cover the activities of those employees that companies might not call representatives.

For the purpose of this paper these employees will be referred to as medical and scientific liaison executives and the like. An important factor is whether the activities are reactive or proactive or a mixture of both.

The following are examples of the types of activities that such employees might undertake and the relevant clauses of the Code when considering each activity as a discrete entity.

a Provision of disease area information

If the medical and scientific liaison executives and the like call upon health professionals and/or other relevant decision makers to discuss diseases, and there is no reference either direct or indirect to specific medicines, then this activity is covered by an exemption to the definition of promotion given in Clause 1.2. This states, *inter alia*, that the term promotion does not apply to information relating to human health or diseases provided there is no reference, either direct or indirect, to specific medicines.

If specific medicines are referred to either directly or indirectly, then the activity could not take the benefit of that exemption and would be likely to be seen as promotion of those medicines. It would be a breach of Clause 3 to promote the product or the indication before receiving the relevant marketing authorization.

In exceptional circumstances it might be acceptable to provide a very general explanation as to the company's interest in the disease area without such an explanation being viewed as promoting an unlicensed indication or medicine.

b Promotion of licensed products and indications

If, as part of their role, the medical and scientific liaison executives and the like promote licensed products and indications then they are covered by the Code including the specific requirements for representatives (Clauses 15 and 16). Companies will need to be extremely careful to ensure that such promotional activity is very clearly separated from the non-promotional role of a medical and scientific liaison executive and the like. This distinction must be clear to health professionals. The medical and scientific liaison executives and the like must not carry out a promotional role and a non-promotional role in the same call and generally promotional and non-promotional activities should be performed by separate staff.

c Provision of information on products or indications that are not licensed

The basis for such activity is twofold.

Firstly, the exemption to the definition of promotion given in Clause 1.2. This states, *inter alia*, that the term promotion does not apply to replies made in response to individual enquiries from members of the health professions or other relevant decision makers or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they relate solely to the subject matter of the letter or enquiry, are accurate and do not mislead and are not promotional in nature. Relevant supplementary information states that replies intended for use in response to enquiries which are received on a regular basis may be drafted in advance provided that they are used only when they directly and solely relate to the particular enquiry. Documents must not have the appearance of promotional material.

Companies must be able to demonstrate that the medical and scientific liaison executives and the like are responding to unsolicited, specific, individual enquiries from health professionals and/or other relevant decision makers. Misleading or inaccurate information used to respond to an unsolicited enquiry would be in breach of the Code. Material would also be in breach of the Code if it went beyond that needed to answer the enquiry and/or had the appearance of promotional material.

The supplementary information to Clause 3, Marketing Authorization, states that the legitimate exchange of medical and scientific information during the development of a medicine is not prohibited provided that any such information or activity does not constitute promotion which is prohibited under this or any other clause. Companies must ensure that such activities constitute a genuine exchange of information and are not promotional. Documents must not have the appearance of promotional material. It should be borne in mind that it would be a breach of the Code if non-promotional information on products or indications that are not licensed was used for a promotional purpose.

If a company is producing information on an as yet unlicensed indication for a product that has a marketing authorization, for example at a company symposium at a learned society's meeting, this must be a genuine legitimate exchange of medical and scientific information during the development of that medicine, involving debate which would enhance the current state of scientific knowledge. To avoid being seen as the dissemination of data to expand the product's use, ie promotional and in breach of the Code, the activity must not be a one way flow of information.

As stated above it is likely that the proactive provision of information about unauthorized medicines and/or unauthorized indications by pharmaceutical company staff calling upon health professionals is promotional and thus prohibited.

d Provision of information on products or indications that are not licensed but which have significant budgetary implications

Such activities are covered by the supplementary information to Clause 3.1, Advance Notification of New Products or Product Changes which May Significantly Affect Expenditure.

If the product does not have significant budgetary implications for the prospective purchaser then any proactive provision of information, budgetary or otherwise, is likely to be seen as promotion. It would be a breach of Clause 3 to promote the product or the indication before receiving the relevant marketing authorization.

e Advice regarding the role and activities of medical and scientific liaison executives and the like

The following is intended to assist companies:

- i) The overall governance of medical and scientific liaison executives and the like should be the responsibility of the medical director or similar, irrespective of reporting lines, rather than the commercial side of the company.
- ii) Medical and scientific liaison executives and the like must be appropriately qualified and trained. They must be fully conversant with the requirements of Code and the guidelines on company procedures included in the Code of Practice booklet.
- iii) The provision of medical and scientific information about unauthorized medicines and/or indications and other non-promotional activities must be kept completely separate from promotional activity. Ideally medical and scientific liaison executives and the like should not call upon the same people for both promotional and non-promotional purposes and generally promotional and non-promotional activities should be performed by separate staff. The differences between a medical and scientific liaison executive and the like and a sales representative should be obvious to those receiving such calls.

Medical and scientific liaison executives and the like can arrange meetings to present information in response to an unsolicited, specific, individual enquiry about an unlicensed product or indication. Unsolicited questions at that meeting about a licensed product or indication can be answered but the discussion should be limited and non-promotional in nature and the enquirer should be brought back to the main topic of the meeting. Medical and scientific liaison executives and the like should not set out to use a non-promotional meeting to also promote licensed indications and/or products.

Such an enquiry might be from a group of health professionals where one person has asked the question and wants a number of colleagues to hear the answer. This needs to be treated with care and certainly the medical and scientific liaison executive and the like should not suggest that others might be interested in the answer. It should be an unsolicited suggestion from the enquirer.

- iv) Relationships with other company staff such as medical/generic representatives must be carefully documented and explained to all parties.

The non-promotional role of medical and scientific liaison executives and the like could be compromised by the presence of other company employees.

- v) Medical and scientific liaison executives and the like can train other employees such as medical/generic representatives provided that the training materials meet all the relevant requirements of the Code. Particular attention is drawn to Clause 15.9 relating to representatives' briefing material and the need to have such material certified in accordance with Clause 14.
- vi) The remuneration of those employed as medical and scientific liaison executives and the like must not be linked to the number of enquiries answered or the number of visits,

meetings etc but a bonus scheme linked to the percentage of enquiries or visit requests completed may be acceptable. Remuneration should not be linked to sales in any particular territory or place or to sales of a specific product or products and, in particular, may not include a bonus scheme linked to such sales. Bonus schemes linked to a company's overall national performance, for example sales in the UK, may be acceptable.

- vii) Materials for medical and scientific liaison executives and the like to use in a non-promotional context, such as presentation materials, internal instructions etc, must be accurate, not misleading and must not have the appearance or tone of promotional material. Materials should meet the requirements of the Code and in this regard particular attention is drawn to Clauses 7.2, 7.3 and 7.4. Non-promotional material must not be used for a promotional purpose. Companies can prepare presentations etc in advance. Other relevant employees should be clearly instructed about the role of the medical and scientific liaison executives and the like and the referral of enquiries to them.

Instructions need to be given as to the procedure for tailoring prepared materials to answer a specific enquiry. Documentation, such as a form for the health professional to complete outlining the nature of the enquiry, would be helpful if a company was called upon to demonstrate that an enquiry was unsolicited.

The materials must be examined by companies to ensure that they do not contravene the Code or the relevant statutory requirements, as recommended in the supplementary information to Clause 14.3 for material used by companies that is not intended as promotional material *per se*.

6 INFORMATION TO THE PUBLIC

Clause 26.2 sets standards for the provision of information to the public directly or indirectly, such as via a journalist. These include a requirement that statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine.

The supplementary information to Clause 26.2, Information to the Public, states that reactive information may be supplied to the public in response to a direct request and must be limited to that information necessary to respond to the request. The principles set out in the supplementary information to Clause 1.2, Replies Intended for Use in Response to Individual Enquiries, would be relevant. A solicited request for information about prescription only medicines may be in breach of Clause 26.

Clause 26.4 states that requests from individual members of the public for advice on personal medical matters must be refused and the enquirer recommended to consult his or her own doctor or other prescriber or other health professional. The supplementary information refers to the possibility of providing information to the patient's health professional for discussion rather than directly to the patient.

Of course the promotion of prescription only medicines to the public would be a breach of Clause 26.1.

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