
Working Party Report

Self-medication of antibacterials without prescription (also called ‘over-the-counter’ use)

A report of a Working Party of the British Society for Antimicrobial Chemotherapy

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The availability of antimicrobial agents for self-medication may increase and could include antibacterial agents for oral or topical use. Wholesale deregulation of antibacterials would be undesirable and likely to encourage misuse of classes of agents currently important in the management of serious infections. Changed regulation from Prescription-Only Medicine (POM) to Pharmacy (P) medicine of selected agents with indications for short-term use in specific minor infections and illness is likely to have advantages to the user. However, safeguards to their use would need to be included in the Patient Information Leaflet (PIL). Agents and indications for self-medication are discussed. Any alteration in licensed status from POM to P will require careful risk–benefit assessment, including the likely impact on bacterial resistance. Safety issues also include concerns relating to age of the user, pregnancy, underlying disease and the potential for drug interactions. The importance of appropriate information with the PIL is emphasized, as is the role of the pharmacist, while ways of improving adverse event notification and monitoring are discussed. The paucity of good denominator-controlled data on the prevalence of in-vitro resistance is highlighted, and recommendations for improving the situation are made. There are currently no levels of resistance accepted by regulatory bodies on which to base a licensing decision, be it for granting a product licence, renewal of a licence or a change in licensed status from POM to P. Due consideration should be given to: the validation of user-defined indications in comparison with those medically defined; the enhancement of pharmacy advice in the purchase of such agents; improved safety monitoring; the establishment of systematic surveillance of susceptibility data.

Introduction

The Working Party responsible for this report was convened in mid-1996 in response to the interest engendered by the increase of previously prescription-only non-antibiotic drugs then available for self-medication through pharmacies, and the likelihood that future regulatory changes might also affect antibiotics. The precedent of topical antifungals and antivirals and the availability of

systemically active fluconazole supported this view. During the two years in which the Working Party debated, drafted and finalized its report there has been a hugely increased public and professional awareness of the importance of the increasing resistance of bacteria to antibiotics. A Select Committee of the House of Lords has recently reported on this topic, as has the Department of Health's Standing Medical Advisory Committee very recently. The former has unequivocally rejected the notion that antibacterials

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Working Party Report

should be made available for self-medication, and this was echoed in a public statement by the Chief Medical Officer. None the less, we believe that a limited case can be made for some licensing of over-the-counter (OTC) antibacterials, albeit for very clearly defined indications and formulations. The Working Party shares the concerns that have been voiced about the potential harmful effects of OTC licensing of antibacterials. It discussed this dilemma and came to the conclusion that, on the balance of the likely benefit to patients and the potential harm to the community from increased resistance, its recommendations were modest and well-founded in logic and science. In examining the advantages and disadvantages of any regulatory change to allow self-medication with antibiotics, we have clearly identified circumstances in which selected agents might be made available as short treatment courses. However, the caveats identified clearly recognize the current limitations of making drugs available for self-purchase through pharmacies.

The Working Party is aware that some aspects of its report are controversial and wishes to emphasize that its opinions are its own and not those of the British Society for Antimicrobial Chemotherapy (BSAC) or of other professional bodies to which members of the Working Party belong. It also believes that its opinions are justified on the basis of available evidence, and will be pleased to receive comment on them.

Current regulatory position

The legal classification of medicines and the ways in which they are made available to the public differs internationally. Table I defines the classifications used in the UK and how these determine public access to medicines through

pharmacies or other retail outlets. In common with most of Europe, but in contrast to the USA, all medicines newly released from prescription control in the UK can only be sold in pharmacies under the supervision of a pharmacist. In other words, free selection by the patient is not allowed; this differs from the arrangements for agents classified as General Sale List (GSL), which can be freely purchased without professional intervention.

In the UK an exemption to a Prescription-Only Medicine (POM) order may be requested by the Marketing Authorization (MA) holder. Non-prescription use, whether under Pharmacy (P) status or for a medicine on the GSL list, is commonly restricted to: those indications which can easily be recognized by a patient; particular dosage forms; limited duration of therapy (i.e. a defined pack size or number of doses); certain patients only (e.g. age group limits, absence of stated concomitant diseases). It is also common for additional warnings and precautions to be added to the Patient Information Leaflet (PIL) which refer specifically to P uses. Usually there are separate PILs for POM and P uses. The European Union (EU) directive 92/26/EEC provides two classifications—medicinal products subject to medical prescription and medicinal products not subject to medical prescription.¹ Article 3 of the directive provides criteria for classifying a medicinal product as subject to medical prescription. However, the supply of human medicinal products varies between member states and products sold without prescription in certain member states can be obtained only on medical prescription in others.

In an effort to facilitate the harmonization of prescription-only and non-prescription products throughout the EU, the European Commission (EC) has recently issued guidelines which establish criteria for switching prescription-only products to non-prescription status.

Table I. Definitions of licensing categories for the purposes of this report

Category	Definition
Prescription-only medicines (POM)	These meet the criteria of directive 92/26/EEC. They therefore include: relatively new medicines that require medical monitoring of activity and adverse effects, other medicines which require medical supervision for their safe use, medicines which are frequently used incorrectly leading to human health risks and all medicines which are normally prescribed to be given parenterally. POM medicines may not be promoted to the public.
General sale list (GSL)	These contain ingredients which can be sold from any lockable shop. Typically the main outlets for these are grocery stores, drug stores and health-food shops; self-service of these products is allowed. Products which can be sold in this way include small packs of analgesics containing aspirin, paracetamol and ibuprofen, most antacids, simple cough mixtures, throat pastilles and antiseptics. Some EU countries do not have medicines equivalent to the GSL status
Pharmacy medicines (P)	These can only be sold from pharmacies under the supervision of the pharmacist. Products recently removed from prescription control fall into this category. They may have restrictions on age of patients, indications, pack size and duration of treatment compared with their use on prescription. Self-selection of these medicines is not allowed so they can only be supplied from 'behind the counter' in pharmacies.

Over-the-counter antibacterials

A recent Medicines Act Leaflet² provides a clear account of how an application to change legal status is evaluated in the UK. The availability of non-prescription medicines has previously been discussed.³⁻⁷ The World Health Organization (WHO) also describes the benefits of self-medication in recurring or chronic illnesses.⁸

The principles which should govern a change of legal status to self-medication are thus well established. How these general considerations relate to antimicrobials poses some particular and important questions.

The current regulatory atmosphere in Europe, and particularly in the UK, would appear to be positive towards deregulation of licensing.⁹⁻¹¹ An increasing number of drugs have been switched from POM to P in the UK (five between 1983 and 1990, and some 41 since) and it is natural that antimicrobials might be considered similarly. In developing this report it was decided to focus entirely on antibacterials, while recognizing that both antiviral and antifungal agents are currently available for self-medication, the principle thus being established. This was because the potential for greater use or misuse is more likely with antibacterials, and antibacterial resistance is currently of major public and professional concern. The principles we have set out for the use of antibacterials for self-medication could, however, also apply to other classes of antimicrobials.

The EC has defined the characteristics of a drug which justifies POM status.¹ This directive indicates broadly that medicines should be available without a prescription unless there is a good reason why this should not be the case. Many drugs for treating infections could qualify on safety grounds by these criteria. However, antimicrobial drugs have particular characteristics. (i) If they are used incorrectly the individual patient may not be harmed, but with excessive use in the community they may ultimately have reduced usefulness because of drug resistance. (ii) In the lay mind an 'antibacterial' may be viewed as suitable for all infections (and many patients will in the past have been prescribed the same antibacterial for a variety of illnesses). Therefore the agent may be inappropriately used, treatment courses fail to be completed or the drug hoarded and inappropriately used in the future by the purchaser or another person.

A number of antimicrobials are currently available for self-medication in the UK (Table II). The majority of the preparations are for topical application; only fluconazole and the antimalarials are systemically active. No systemically active antibacterial is currently available for self-medication.

At present the only health professionals, other than medical practitioners, who are able to prescribe antibacterials are dentists, who can prescribe a limited number of oral antibacterials detailed in the *Dental Formulary*. It has recently been proposed that chiropodists might supply oral flucloxacillin and erythromycin.¹² They can currently supply some local antifungals.

In view of the possibility that pharmaceutical companies might seek approval for antibacterials having self-medication status, the Council of the BSAC (which has a considerable record of convening working parties on matters of current moment) set up a Working Party to consider the scientific and professional issues surrounding the possible sale of antimicrobials for self-medication. In the context of this report 'over-the counter' means self-medication with P-status medicines; we did not contemplate the availability of antimicrobials on the GSL. Thus the deliberations and conclusions of the Working Party, although addressing the UK situation, could have applications in other countries with medicines on a status equivalent to Pharmacy in the UK, whilst the general principles clearly have international application. Currently we believe that no other professional body is producing a similar report.

Terms of reference

- (1) To review and report on the scientific and professional issues pertinent to the wider availability of antimicrobial substances through non-prescription arrangements.
- (2) To consider specifically:
 - (a) oral and topical therapeutic agents;
 - (b) indications which might be suitable for self-medication, and to evaluate the suitability of specific infections for self-medication with antibacterial agents;

Table II. Some antimicrobial agents available for self-medication in the UK (1998)

Oral	
urinary antiseptic	hexamine hippurate
antifungal	fluconazole
antimalarials	chloroquine, proguanil
antihelminthics	piperazine, mebendazole, niclosamide
Topical	
antifungals	clotrimazole, miconazole, tolnaftate
antiviral	acyclovir
antiseptics	a wide variety

- (c) the characteristics of antimicrobials which might or might not make them suitable for self-medication, and to consider possible specific classes of antimicrobials suitable for use in various indications;
 - (d) the possible benefits and disadvantages specific to OTC antimicrobials for self-medication;
 - (e) which co-morbidities and other drug prescriptions might exclude or modify the availabilities of drugs for self-medication;
 - (f) recommendations on what might usefully be included in PILs;
 - (g) whether systems could be recommended which would make antimicrobials safer for self-medication;
 - (h) recommendations to assess the potential ecological impact of the availability of antimicrobials for self-medication.
- (3) Specific products would not be named except where this is predicated by there being only one member in a class of antibacterials.

Aims of the Working Party

Thus the aims of the Working Party were to produce a report, subsequently specific to antibacterials, on the issues relevant to any possible switch from POM to P status that would be informative to licensing authorities, the pharmaceutical industry, pharmacists, prescribers and the public. It would not consider in detail general issues regarding POM-to-P switches which are well described elsewhere.¹³ The terms 'non-prescription medicine' and 'self-medication' are all-embracing and avoid the potential confusion that surrounds existing variations in international nomenclature, especially in the use of the term 'over-the-counter'.

Methods of working

The convenors of the Working Party (Professors R. G. Finch and D. S. Reeves) invited the members of the Working Party on the basis of their expertise in drug regulation of antibacterials and specialist areas of medicine likely to be most affected by the availability of antibacterials for self-administration. Members were chosen not as being representative of any particular interest group but for the knowledge they could bring.

Contributions to the deliberations of the Working Party were canvassed through the BSAC and a letter published in the *British Medical Journal*.¹⁴ A leading article and a letter in the *Pharmaceutical Journal* also provided an opportunity to respond and thus to inform the pharmacy profession of the existence of the Working Party.¹⁵⁻¹⁷ Three letters were received at this stage from physicians and one from a pharmacy student.

During 1997 opinion on the then current draft was sought from experts in a number of relevant fields. These included paediatrics, dermatology, ophthalmology, medi-

cal microbiology, drug regulatory affairs, adverse reaction monitoring and organizations representing commercial interests. These views were taken informally and not as representing any particular interest or organization, and it is for this reason that their names are not cited. We are very grateful to these experts for giving up their time in contributing their expertise in this way.

Potential benefits of self-medication with antibacterial drugs

Potential benefits can be viewed as those arising with any drug and those arising with antibacterials:

Potential benefits arising with any drug

The availability of drugs by purchase for self-medication could result in a number of advantages to varying degrees.

- (1) Patients would have a greater choice of access to healthcare both in the way it is delivered and at a time and place convenient to them. At the present time the provision of healthcare is medically led and controlled, particularly in relation to the provision of drugs for the management of infections. Many of the current arrangements and systems for healthcare delivery lack flexibility when dealing with minor or self-limiting infectious illness which may arise at any time, including weekends, or when the patient is away from their normal place of residence. Social changes in relation to patterns of work, including shift work, difficulties of access to general practitioners (GPs), the rise of single-parent households and the economics of ill health from loss of earnings, job insecurity and the cost of child-minding have all added to the demands for greater flexibility when dealing with minor illness, which are perceived as having a low medical priority in an overburdened health system. In addition there is a culture which puts an increasing emphasis on personal responsibility for healthcare which would be furthered by increasing availability of self-medication.
- (2) GPs may gain from having fewer consultations for minor illness and in turn have more time for more cost-effective interventions.
- (3) Pharmacists would have a further opportunity to use their professional knowledge and develop their range of services to the public.
- (4) The pharmaceutical industry would be in a position to exploit a new marketing opportunity. A healthy pharmaceutical industry is also important for the economic wellbeing of the nation and hence government continues to encourage the legitimate market activities of the industry which, in turn, sees opportunities from a relaxation of the current attitude to self-medication.

- (5) The government could be relieved of some costs of antibacterials obtained on National Health Service (NHS) prescriptions, although it is estimated that the savings are unlikely to be large.¹⁸

Potential benefits specifically for antibacterials

Infections are illnesses which usually present acutely. Patients may therefore benefit specifically from the greater immediacy and convenience of access to antibacterials (as discussed above). This could potentially shorten the period of illness, reducing both the length of symptoms and the period of infectivity. The OTC availability of treatment for vaginal candidosis and herpes labialis probably shortens the delay between onset of symptoms and start of effective treatment. This is particularly important for herpes labialis, because delay in treatment significantly diminishes its effectiveness. Both of these infections are recurrent, have quite distinct clinical symptom complexes and are easily recognized by patients who suffer them. In contrast, most bacterial infections are exceedingly difficult to diagnose clinically; this applies particularly to respiratory tract infection, the commonest type of bacterial infection requiring antibiotic treatment in the community.^{19,20} It is only patients with confirmed bacterial infection who benefit from antibiotic treatment.²⁰ Therefore, the argument that OTC availability of antibiotics will improve access to effective treatment for respiratory symptoms is not very compelling, given that less than a quarter of patients with symptoms can derive any benefit from antibiotic treatment.

Another argument used to support OTC availability of antibiotics for respiratory symptoms is that this will reduce the number of patients with communicable diseases who attend doctors' waiting rooms. We are not aware of any evidence to support this assertion and the same aim may well be achieved by strategies which reduce antibacterial prescribing by GPs, which have been shown to reduce the number of patients who consult their GPs with minor respiratory symptoms.²¹

Consensus view. The availability of antibacterials for self-medication might result in considerable benefit to individual patients and reduce the burden of minor illness on health services, but only if the infections being treated can be reliably identified from characteristic symptom complexes.

Potential disadvantages of self-medication with antibacterial drugs

Among the possible adverse consequences of self-medication are those to individual patients, which include misdiagnosis and missed diagnoses, misuse of drugs (including unintentional access by children) and increased risk of adverse reactions and drug interactions, particularly in

children, the elderly, the pregnant and those with pre-existing disease. Antibacterial use is, however, unique in that it has the potential to harm society in general (as well as individual patients self-medicating) by decreasing sensitivity to antibacterials. There is also the potential of lost data on the epidemiology of resistance should antibacterial use extend beyond the existing prescribing arrangements.

Possible adverse consequences for individual patients

Accuracy of diagnosis. Misdiagnoses could have several adverse consequences. These include: (i) the partial or complete failure to treat an infection (such as therapy for presumptive urinary tract infection (UTI) when the patient has a sexually transmitted disease); (ii) the failure accurately to identify or treat the presenting infection (such as otitis media complicated by meningitis); (iii) exposure to the risks of antibacterials without benefit when no treatable bacterial infection is present; (iv) possible increase in the number of patients receiving antimicrobials with consequent increase in the ecological pressure for resistance; (v) failure to recognize that an infection might be a manifestation of underlying disease (e.g. sepsis in diabetes mellitus).

Thus to advocate a change in licensed status of antibacterials there must be reasonable certainty that the diagnosis and treatment of infections will not be significantly compromised over treatment by prescription. It is important to realize that, unlike action by a GP, the pharmacist is not making a clinical or presumptive microbiological diagnosis. Rather, the pharmacist's role is to assist the purchaser in deciding whether the criteria are met for which non-prescription use of the medicine is approved. For this reason the Working Party considered that only infections which had symptomatology strongly linked to particular infection, and which in current medical practice would often result in the empirical prescribing of a similar antibacterial, should justify consideration for self-medication.

It is acknowledged that microbiological diagnostic tests will not be available to self-medicating patients, unlike to GPs. However, it is also known that few GPs take specimens from patients for whom they prescribe antibacterials. For example, in managing acute UTI it is common practice to treat empirically without taking a specimen.

There is a difficulty in that pharmacists helping the public in self-diagnosis in most retail pharmacy premises are not able to provide sufficient privacy. Patients who need to describe their symptoms confidentially may thus withhold important information. A particular area of concern, for example, is the misdiagnosis of sexually transmitted diseases, whose symptoms might mimic UTI, although the potential for this misdiagnosis must be at least as great for vaginal candidosis, for which P status for topical and oral antifungals is established. The possibility of using validated simple questionnaires for self-completion in the pharmacy should be considered. When it

is not clear that an indication for self-medication exists, it is usual for the pharmacist to decline to sell the medicine and to recommend medical assessment to the patient. In the UK, with its P-only arrangement for self-medication with H₂ antagonists, it is thought that the conservatism of pharmacists has resulted in lower sales than might have been otherwise anticipated from sales in the USA, where these drugs can be self-selected, as with the GSL in the UK.

Possible increases in adverse reactions and drug interactions. Antibacterials for oral administration have a relatively good track record of safety. The serious and non-serious adverse events profiles for many antibacterial agents available for oral administration and their potential for clinically significant drug interactions indicate that the risk–benefit relationship might be appropriate for non-prescription use. Only antibacterials with a well-established safety record should be considered for self-medication. Specific contraindications should be ascertained by the pharmacist although they would be disadvantaged compared with a GP because of the lack of availability of any medical records. However, the PIL offers an important vehicle of information to the patient since it reflects, as required by the EU, all the contraindications, warnings and precautions listed in the Summary of Product Characteristics (SPC) and gives advice on use in pregnancy and lactation. The pharmacist also has the opportunity to discuss these with the purchaser. Reporting by pharmacists of adverse drug reactions and adverse events should be encouraged, and this is now facilitated by the proposed extension of the ‘yellow card’ scheme to pharmacists. Patients should be encouraged to tell their GP, as usually recommended in the PIL, about antibacterials used for self-medication since this may influence the choice of a subsequently prescribed antibacterial.

Potential for ecological harm

Increased bacterial resistance. There is clearly a possibility that making some oral antibacterials available for self-prescription could lead to increased bacterial resistance. There is currently widespread concern throughout the world about increasing resistance to antibacterials. Excessive, inappropriate and indiscriminate use of antibacterials in humans has been cited as a possible cause, but some half of the worldwide use of antibacterials is in veterinary medicine and animal husbandry. The concerns have been voiced in a number of forums, such as the 1996 WHO Annual Report.²² More recently, other organizations (e.g. The Wellcome Foundation, the House of Lords, the Department of Health, and The Centers for Disease Control, USA) have developed initiatives to examine the problem.

In considering resistance it is important to be clear about what is meant by the term. For the purposes of this report, resistance is defined as a decrease of in-vitro susceptibility

to an antibacterial to the extent that therapy is likely to fail when it is used clinically for a recommended indication and at the usual dose. This is to distinguish it from the degree of in-vitro resistance which might arise from genetic or adaptive changes. However, we also consider that a reduction of in-vitro susceptibility to a lesser degree (i.e. to a degree which does not cause failure of therapy) is an important consideration since it may presage a greater loss of susceptibility.

We also recognize that resistance is largely identified by in-vitro test methods. Lack of standardized methods and international variations in breakpoints cause confusion when collecting and comparing epidemiological data and correlating in-vitro susceptibility with clinical outcome.

The Working Party also considered whether it is possible to demonstrate a proven causal link on a population basis between antibiotic usage and resistance and concluded that this was unlikely in the foreseeable future. The reasons for this are the difficulties encountered in interpreting largely retrospective and uncontrolled in-vitro data for hospital settings, and the near impossibility of conducting prospective controlled studies. This has been well discussed by McGowan.²³ None the less there are a few useful examples in which resistance has clearly been associated with widespread usage (e.g. *Streptococcus pyogenes* and erythromycin) and the trend reversed subsequent to reducing the usage,²⁴ although it is likely that resistance to macrolides is not typical of other classes of agents in the ease with which it is acquired or lost. For the purposes of this report we accepted that the emergence of resistance was a function of exposure to antibacterials in terms of individual treatments, total usage and the passage of time, although these factors affect different pathogens and drugs variably. It should also be appreciated that when a POM licence is granted there are presently no restrictions placed on the global amount of antibacterial which may be prescribed. There is therefore a logical inconsistency in restricting change from POM to P status solely on the grounds that the amount of drug used might increase.

The Working Party considered the question of whether the availability of antibacterials for self-medication would lead to an increased use. This has to be considered in the context of individual agents and infections. Clearly if the indication were (for example) for a sore throat, then increased usage is likely to occur since many GPs do not prescribe an antibacterial for this indication. The likelihood of an increase was less clear with, say, uncomplicated UTI since the symptoms may indicate an antibiotic-responsive infection and most GPs would prescribe for them. It is accepted that some patients might not bother to go to their GP and the symptoms would resolve spontaneously; in these circumstances the availability of effective agents might lead to self-medication with an antibacterial. It is also known that some patients keep unused antibacterials which they use on future occasions, such that prescription numbers do not presently represent the totality of episodes

of exposure to antibacterials. The Working Party could not quantify the possible increase in use from self-administration but felt it likely to vary by drug and indication. The overall impact might be small in the context of the total prescription market and the use of antibacterials in animals in the human food chain.

Against this view is the fact that commercial considerations might result in vigorous promotion and expanded use to ensure commercial viability of any alteration in the licensed arrangements for a product.

It is possible that self-medication may alter the type of antibacterial used for the good. For example, if agents used solely for UTI (see below) were released for self-medication of acute UTI then this could result in a lowering of the number of prescriptions of β -lactam agents and trimethoprim which are used systemically for other, sometimes more serious, infections. This might be beneficial to the general problem of resistance. Furthermore, the prescription of fewer β -lactams might result in less superinfection with *Clostridium difficile* and *Candida* spp. In addition, since the Working Party thought that any antibacterials for self-medication of UTI should be clearly for short-course or single-dose therapy, and since some GPs still prescribe longer courses for UTI, it is possible that the total number of days of exposure to antibacterials may be reduced by self-medication. There is a problem here, however, since some antibacterials for UTI have licensed indications which give longer courses, which would necessitate a change to the SPC at the time of the POM-to-P switch; this would require submission of new efficacy data to support any change in the proposed duration of therapy. Whether an applicant would wish to incur the additional expense would clearly be a commercial decision.

The Working Party considered whether increased use from self-medication might have a significant impact on the prevalence of bacterial resistance in general. As with current antibacterial usage by prescription, it would be difficult to demonstrate a proven causal link between antibacterial usage resulting from self-medication and resistance to antibacterials because of the multifactorial nature of the problem and the difficulty of controlling for confounding factors. These include differing patient populations, inadequate denominator data, changes in infection-control practices, unpredictable or undetected clonal spread of resistant bacterial strains, and selected data from units in which the high proportion of patients with complex conditions makes them more liable to acquiring infection with resistant bacteria.

Bacterial resistance is undoubtedly increasing among some community pathogens as well as hospital-associated ones in countries where antibacterials are available only on prescription. Data from countries with poor control on access to systemically available antibacterials might be taken to support the claim that either non-regulation or failure to implement regulated use of such agents may promote greater bacterial resistance, but it is difficult to

extrapolate the position in these countries to the kind of deregulation that might be applied in the UK.

An almost inexorable rise in bacterial resistance to antibacterials has, however, undoubtedly occurred even in regions with physician-controlled use and high standards of hygiene, as in western Europe, North America and Australasia.^{25,26} It would be difficult to argue that the rise would have taken place in the absence of antibacterial usage but whether greater availability of a limited number of antibacterials for self-medication would promote more resistance is unclear. A high level of antibacterial use may continue for many years without overt increase in resistance. However, once this does occur, resistant strains can spread rapidly as, for example, with *Streptococcus pneumoniae*. The Working Party accepted for the purposes of its deliberations that with the passage of time the cumulative rise in the use of an antibacterial may eventually lead to a greater prevalence of bacterial resistance to it. The extent of this would, however, probably vary by antibacterial agent and pathogens and the time in which this might occur is unpredictable. Much would depend on the nature of the antibacterials used for self-medication and the infections treated.

The Working Party considered the question of what change in the level of resistance to a particular antibacterial for self-medication should influence, if at all, the status of its licence. It decided that this would depend on the antibacterial and the indications, particularly with regard to the seriousness of the latter, as well as the quality of the information on which altered susceptibility was assessed. At present the influence of low-level resistance on the outcome of therapy is poorly understood for many antibacterials, target pathogens and indications. The Working Party did consider that monitoring resistance to an agent released for self-medication could be a condition of licence and that these data would be used at licence review. However, this would require precise information on the target pathogens within the population to be treated and in the geographical area covered by such licensing. Within the EU this clearly presents difficulties, not least because the pattern of resistance to many antibacterials differs in the various member states. Furthermore, there are no robust guidelines as to what level of in-vitro resistance translates into predictable clinical failure and in turn should invoke a regulatory response.

Alterations in susceptibility of target bacteria has not been a major consideration for drug licensing authorities, including the UK. The major concerns remain quality, efficacy and safety of medicinal products which are a balance of benefit and risk according to the indications of use. However, the problems created by methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, multiply drug-resistant *Mycobacterium tuberculosis* and penicillin-resistant pneumococci are altering this traditional attitude. A new EU guideline²⁷ recommends that information on susceptibility data of target

pathogens should be included in the SPC for antibacterial drugs; this will be applicable to new chemical entities with EU licences and not to POM-to-P switches (which are a national responsibility). Such information is likely to be of limited scope since it is intended to give a general view of the prevalence of resistance of specific pathogens to a licensed agent across Europe. Furthermore, it is not stated how these data should be collected, defined and validated in relation to dosage recommendations. There is a risk that such data could be exploited commercially in promoting one agent in relation to its competitors. The impact of this legislation is awaited with interest.

Resistance to antibacterials has reached high levels with certain POMs (e.g. with ampicillin and *Escherichia coli* causing UTI) yet this indication still remains on the data sheet. There would be an inconsistency if restrictions were placed on P-status antibacterials and not on those available by prescription since we considered that the same principle should apply to both. Indeed, one might argue that greater leniency be given to P-status antibacterials since they would be used for less serious indications.

During the treatment of individual patients it was thought unlikely that bacterial resistance would occur in the responsible pathogen any more frequently from self-medication than with prescribed medication. The antibacterial would be taken by the same route and for a similar time. Indeed, it is possible that compliance with self-medication may be better because of motivation in self-care and emphasis on it within the PIL. More important than resistance arising in the target pathogen is the selection pressure on the normal flora since resistant bacteria selected in this way can spread to other persons.

With regard to risks of promoting antibiotic resistance, it was considered that certain orally active antibacterials from classes of agents frequently used to treat serious infections should not be available for self-medication, since the possible risk of societal harm was considered to outweigh the potential benefits to individual patients. Thus we recommend that all oral β -lactams should be excluded because of their major importance in treating serious or common infections and the propensity of target pathogens to exhibit readily diverse resistance mechanisms. Ideally, only antibacterials with specific indications should be considered for self-medication (eg. nitrofurantoin for acute UTI). Before a particular agent could be recommended for self-medication, data on cross-resistance (including linked resistance) to other antibacterials used in serious infections should be available.

Owing to the potential for increased resistance, the Working Party supports the commissioning of proper surveys of the prevalence of resistance in the target pathogens before the introduction of an antibacterial for self-medication. These should be supported by the company marketing the antibacterial but carried out independently to a scientifically acceptable protocol. Currently surveys of antibacterial resistance in the community generate poor

data in that the sample population is ill-defined (e.g. for UTI it is usually not known whether these are recurrent infections or whether the patients have recently received antibacterials), there is usually a lack of denominator data, and clinical outcomes are ignored. In-vitro susceptibility may also be judged against inappropriate breakpoints or be only determined semi-quantitatively (e.g. by disc testing). There are inconsistencies in the definition of in-vitro resistance, particularly between countries. Ideally the prevalence of resistance should be determined by carefully designed surveys of defined patient populations in limited geographical areas (but representative of the territory in which the antibacterial will be promoted) in which the denominator data are also defined. Clearly such data would be valuable before the granting of a MA for a POM as well as one for self-medication. Data on utilization of the relevant antibacterial for the same geographical area should also be available so that comparisons can be made between antibacterial usage and resistance in defined populations. In the case of self-medication the pack size will contain a single course so data on the number of courses and total dose of antibacterial taken can be assessed reasonably accurately. Any prescription use in parallel could be determined from Prescription Analysis and Cost (PACT) data in England and Wales, or Scottish Prescribing Analysis (SPA) data.

Before self-medication is approved there is thus a major need to acquire sound epidemiological data on baseline community resistance amongst pathogens, which is currently lacking.

The difficulty with such data is how to interpret them both in terms of prevalent levels of resistance and any change that may result. Data on clinical and bacteriological outcomes would also be more valuable but difficult to collect. The generalizability of such selective data to other areas of the UK or beyond would be difficult to determine.

Fears have been expressed that data on the epidemiology of resistance might be lost if patients take self-medication rather than attend their GP. However, the Working Party considered that currently available data are themselves flawed for the following reasons.

- (1) Many GPs do not take microbiological specimens before prescribing antibacterials.
- (2) Some GPs only take specimens for patients complaining of symptoms after a course of antibacterials, while others take specimens before treatment. Without knowing the proportions in each category it is not possible to exclude selection bias.
- (3) Current rates of resistance, while useful for indicating the broad nature of empirical therapy, lack well-defined, consistent denominator data. Apparent trends in resistance rates are therefore subject to selection bias. There are very few data which link information about in-vitro susceptibility to clinical response.

Consensus views. (i) There is strong circumstantial evidence for a causal link between antibiotic consumption and antibacterial resistance. However, the evidence varies by drug, pathogen and time, and precise relationships are difficult to predict. (ii) The OTC availability of selected antimicrobials may increase their total consumption although whether this increase would be significant in the context of total antibacterial use is presently unpredictable. (iii) Introduction of an antibacterial for self-medication should be accompanied by systematic surveillance of resistance to it. However, the manner in which such data should be collected, interpreted and acted upon requires careful definition.

Characteristics of suitable antibacterial agents

In considering a POM-to-P switch of an antibacterial, the Working Party concluded that only selected agents justify consideration and then only following rigorous assessment of their efficacy and safety at the licensed dose and frequency for any proposed indication. The availability of parenteral agents for self-medication is clearly inappropriate. The arguments for self-medication will necessarily, therefore, focus on topical and oral agents for selected use.

As stated above, deregulation of drugs is being facilitated within the EU.¹ Provided safety, efficacy and quality are satisfactory, a primary consideration for evaluating an antimicrobial for self-medication is whether the risk of resistance could be worsened as a result. However, if certain criteria are applied this risk might be reduced. The following might be considered:

- (1) Is the antimicrobial used exclusively or predominantly for a specific infection and, thus, does it have relatively limited indications?
- (2) Is resistance to the drug currently low for those pathogens likely to be implicated in the proposed OTC indication?
- (3) Would selection of resistance to the antibacterial be of consequence to the use of other antibacterials?
- (4) Would the dosage regimen ensure good compliance (e.g. a single dose or a few doses) and the pack size be limited to one course of treatment?
- (5) Is the toxicity profile of the drug sufficiently well-known, and in particular is there a potential for fetal toxicity?
- (6) Is safety in childhood and the elderly established, if children and the elderly are included in the indications?

Consensus view. It is likely that only a very limited number of oral antibacterials will be appropriate for self-medication. These are likely to be well-characterized agents with limited prescription indications, no or minimal cross-resistance to other classes of antimicrobials, and acceptable toxicity profiles.

Possible indications for self-medication with antibacterials

With regard to the indications for self-medication the criteria might include: common conditions; those which are readily recognized by members of the public; those which are not easily confused with more serious conditions; or those which are not life-threatening.

The recurrence of familiar symptoms after an initial diagnosis by a GP, e.g. vaginal candidosis, is a common trigger for self-medication with systemic or topical agents. If patients are given simple guidelines it is likely that they could recognize symptoms of a range of simple recurrent infections which a GP would commonly treat with an antibiotic without microbiological evaluation. Examples include: recurrent uncomplicated UTI in women; conjunctivitis; cough productive of purulent sputum; otitis media; and a variety of superficial skin infections, including acne.

Although symptoms of these conditions may all be recognized with reasonable accuracy, their suitability for self-treatment may be questionable on other grounds. Two factors which will influence this judgement are the likelihood of success if antimicrobial treatment is used empirically and the safety profile (including any potential for drug interaction with prescribed or self-administered medicines) of the antibacterial(s) suitable to treat this range of pathogens. Hence, for example, sore throats and diarrhoea illnesses of short duration are not good candidate indications since antibacterial treatment is only occasionally indicated. Other factors relate primarily to the choice of drug. The suitability of a given infection for self-medication is therefore at least partly dependent on the availability of an appropriate antibacterial for self-medication.

The Working Party considered a number of potential common clinical indications for self-medication and excluded some on the grounds that they were unsuitable. These are discussed in the following sections.

Minor skin infections

Minor skin infection includes secondary infection of cuts and abrasions, boils, paronychia and folliculitis. At present, there are a variety of topical antiseptics and disinfectants available. An anti-infective for self-medication which is not used systemically or is not systemically absorbed might be desirable. It should achieve high concentrations at the site of infection and have been shown to be efficacious. The microbiology of such lesions is relatively predictable and its sensitivity to some local agents reliable. Many topical formulations produce locally inhibitory concentrations even for those pathogens demonstrating in-vitro resistance. Therefore, POM-to-P switches permitting short-course self-medication to minor skin infections would provide effective therapy. Short-course use is emphasized since prolonged use is inappropriate without medical super-

vision and in turn could lead to drug resistance. Despite a lack of hard evidence it was felt that preparations used to manage resistant infections (e.g. MRSA) in hospitals should not be available since their increased use or misuse might lead to an increase in resistance to the agent, which would compromise use in hospitals.

The Working Party concluded that it could not recommend the inclusion of acne as an indication. The reasons were that the agents currently licensed for local therapy are important in systemic therapy (e.g. clindamycin and erythromycin, despite their POM status) or potentially toxic to some people (tetracyclines). Furthermore, acne is a chronic condition requiring long-term therapy for which antibiotics are only one among a range of alternative therapeutic approaches. For these reasons and because immediate accessibility does not weigh as heavily as with some other infections, the Working Party considered that the balance of risk was currently against recommending acne as a possible indication.

Consensus view. Minor skin sepsis could be suitable for short-term treatment by self-medication by local application with an antibacterial not available for systemic use and not used for the control of infection in hospitals. Acne was deemed to be an inappropriate indication.

Urinary tract infection

Short-course or single-dose therapy for uncomplicated UTI is clearly established.^{28,29} We define this as acute dysuria and frequency with accompanying bacteriuria in women aged 16–70 years without known abnormality of the urinary tract and no other known predisposing factors. Many women are familiar with their symptoms and seek an antibacterial from their GP. The availability of oral drugs such as nitrofurantoin or fosfomycin trometamol (an agent no longer available as a POM in the UK), which lack therapeutic systemic concentrations, could provide effective treatment. We are concerned about the risk of adverse reactions to nitrofurantoin which were described in one study to give the highest rate of hospitalizations caused by a community-prescribed drug.³⁰ It is recognized that symptoms of dysuria may apply to other medical conditions. The importance of distinguishing between the upper and lower tract symptoms should be emphasized in the PIL, which should also clearly state what course of action is necessary should symptoms fail to improve, and what other conditions should be considered. It was thought that the lack of urine samples for bacterial investigations before therapy would not adversely affect outcomes in individual patients since therapy by prescription is almost always given for some 2 or 3 days before the results of tests are available. Such investigations are often not requested. The possible loss of epidemiological data is discussed elsewhere. The issue of pregnancy should be included within the PIL, but in the case of nitrofurantoin or fosfomycin it is

not a problem. So long as the agent used was one confined to short-course treatment of UTI the balance of risk would be in favour of making it available for self-medication.

Consensus view. Acute symptomatic uncomplicated lower UTI in adult women, who have already had such an infection diagnosed and treated by a doctor, may be suitable for self-medication with antibacterials. These should be confined to agents indicated only for UTI.

Conjunctivitis

Conjunctivitis is caused by a variety of pathogens only some of which are amenable to treatment with a topical antibacterial. It was felt, however, that self-diagnosis of a non-traumatic acutely inflamed conjunctiva with pus formation was likely to be no less accurate than by a consultation with a GP. The use of a local antibacterial has negligible environmental risk and thus on the balance of benefits its availability for self-medication was supported. The local concentrations in the eye will exceed those necessary to inhibit all strains of pathogens including those demonstrating in-vitro resistance. Patients would be advised to see their GP if vision were affected or there was no prompt response to therapy.

Chloramphenicol may be suitable on ecological and microbiological grounds. Concerns have been expressed that its topical use may carry a very slight risk of blood dyscrasia, but this has recently been refuted and its topical use in this context might therefore be acceptable, although this has been further disputed.^{31–33} The toxicity risk of a fluoroquinolone or an aminoglycoside is also small and these antimicrobials were felt to carry only a very slight ecological risk because of the very small amount of drug applied, although data to support this should be generated. All ecological risks would be little or no greater with self-medication than with prescription use. Aminoglycosides can occasionally cause local inflammatory reactions which might be confused with a lack of response and in turn might make them less suitable than chloramphenicol or a fluoroquinolone for self-medication.

Consensus view. Treatment by self-medication of conjunctivitis with a local antibacterial (a fluoroquinolone) was felt to carry a favourable balance of risks and benefits, and was therefore supported. Although chloramphenicol or an aminoglycoside would also be suitable microbiologically there may be safety reasons for not including them.

Otitis externa

Inflammation of the external auditory meatus, characterized by discharge, itching and local discomfort, might be a suitable candidate for self-medication with a local antibacterial since the high concentrations used would bring most bacterial pathogens within therapeutic reach. How-

ever, worries over the ability of the public to distinguish otitis externa from otitis media or the presence of a perforated tympanic membrane, together with the wide variety of pathogens causing infections, raised sufficient doubts that, on the balance of risks and benefits, the Working Party decided against recommending otitis externa as suitable for self-medication.

Upper respiratory tract infection (including acute sinusitis)

The Working Party felt that upper respiratory tract infection (URTI), including acute sinusitis, deserved careful consideration for self-medication because of the relatively high use of antibacterials in the treatment of these conditions and their generally minor medical importance. Acute pharyngitis is an inappropriate indication for self-medication with an antibacterial because of the relative infrequency of a bacterial cause, and thus large numbers of the public would be exposed to the adverse effects of antibacterials unnecessarily. However, otitis media and sinusitis with a purulent discharge are conditions which frequently give rise to empirical antibacterial prescribing. The availability of an agent such as an aminopenicillin or cephalosporin for self-medication was considered. The most appropriate antibacterials are mostly β -lactams, a class of agent widely used for more serious infections, and to which a number of community pathogens, including those responsible for otitis media and sinusitis, show increasing resistance. For these reasons the Working Party could not support, on the balance of risks and benefits, the inclusion of URTI among the possible indications for self-medication with an antibacterial.

Consensus view. URTI include the most frequent causes of infectious morbidity in the community but only a minority need treatment with an antibacterial. Treatment of any type of URTI by self-medication is likely to increase greatly antibacterial consumption, much of which would have no therapeutic justification. Resistance in the target pathogens is increasing. Furthermore, agents considered suitable are widely used for other indications and have cross-resistance (and linked resistance) with agents used for treating serious infections. We therefore do not recommend URTI as an indication suitable for self-medication with an antibacterial.

Persons for whom self-medication with an antibacterial might be suitable

Self-medication with an antibacterial might be suitable for those with readily identifiable infections for which there is an effective treatment as defined above. In applying for P status for a specific antibacterial, certain members of the target population may need to be excluded. The exclusions might be no different from those for prescription indica-

tions, but could conceivably be widened. For example, children of less than a certain age might be excluded because of the increased difficulty in making a self-diagnosis and taking responsibility for it, although there seems to be no inherent reason why antibacterials should not be available for self-medication in children under the supervision of a legal guardian. There might well be a case for not prohibiting access of children to antibacterials for self-treating acute skin infections and conjunctivitis, and for more ready access to them when a recurrent condition exists, such as UTI, since delays in starting effective therapy often currently occur.

Females are a special group in that they have special problems of interactions (oral contraceptives) and toxicity (during pregnancy and lactation). However, with adequate questioning by the pharmacist and any precautions highlighted by the PIL, the risks should not be greater than for prescribed antibacterials.

Other people who might be excluded include those in whom supervision of any episode of illness might be desirable, for example those with chronic diseases (e.g. end-stage renal failure or diabetes mellitus) or on other drugs (e.g. corticosteroids) which make them more vulnerable to serious infection.

Conditions applying to POM-to-P switches of antibacterials

Product labelling

Detailed requirements for the labelling of products and for PIL content already exist within the EU, supplemented by some regulations specific to the labelling of P-category presentations in the UK. PILs and labels require approval by the UK Licensing Authority. Product labelling and the intervention of the pharmacist in the sale of medicines for self-medication provide important safeguards for the protection of patients. Labels should include the following:

- (1) indications of the symptoms likely to be recognized by the purchaser (photographs might be useful for some indications);
- (2) instructions to the patient to take the medication only for the stated indications;
- (3) advice to complete the full course unless adverse reactions occur;
- (4) details of common and uncommon adverse reactions, described in lay terms;
- (5) details of known drug interactions and contraindications (e.g. oral contraceptives or anticoagulants and certain antibiotics);
- (6) advice to patients to communicate promptly with their GP, preferably by seeing them, if an allergic or toxic response occurs; the accuracy of GP records of allergies currently relies on self-reporting by patients and this seems a modest extension of that responsibility;

Working Party Report

- (7) explanation of how to assess response to treatment;
- (8) the expected course of successful treatment (e.g. for single-dose treatment of cystitis it would be necessary to emphasize that symptoms may persist for up to 3 days, despite successful eradication of bacteria);
- (9) a statement of the necessity for patients to return to their GP if symptoms worsen or persist beyond the expected time;
- (10) advice on how to recognize superinfection (for example, candida vaginitis);
- (11) an explanation of why misuse of antimicrobials (e.g. keeping old medication in the bathroom cupboard) is potentially dangerous; the need to dispose of any unused drug should be emphasized.

Treatment courses should be appropriately packaged to ensure that the dose regimen and duration of therapy are readily adhered to. The PIL should be concise and unambiguous in its instructions and warnings, and available in languages appropriate for the purchaser.

Consensus view. Any agent available for self-medication will need very clear instructions to the patient which cover the issues given above, and will need to be appropriately packed.

Improvement in pharmacy resources

The increasing number of POM-to-P switches has already led to thinking on improvement of pharmacy resources and the Working Party could see no issues specific to antimicrobials. The greater involvement of pharmacists in self-medication has already been supported by further changes in training, continuing professional development and the development of suitable approved protocols. Opportunities to improve professional communications between pharmacists and the medical profession should also be encouraged and might reasonably include on-line computer linkages. The pharmacist may seek information from the patient to assess their suitability for the treatment in question. This can be done using a simple self-administered questionnaire or by direct questioning if this can be done confidentially. There should be adequate provision for dealing with patients whose first language is not English and those who have reading difficulties. Physical arrangements in pharmacies may require further attention so as to permit privacy. The pharmacist is currently not usually in a position to do other than ensure that the most important messages about the medicine's correct use are conveyed. Some key areas would be checking (i) whether the drug is for the use of the purchaser or for someone else; (ii) that the purchaser is in a position to identify correctly the presenting symptoms; (iii) that the purchaser is not taking any medicines that might interact with the drug in question; (iv) that the purchaser knows how to use the medicine (for example, that they can read the label).

Professionally produced protocols would be desirable. In case of uncertainty as to the suitability of self-medication the pharmacist would refer the person to their GP, as is the case for medicines currently available for self-medication. However, it is important to realize that patients may resist such questioning and pharmacists are not obliged to question every patient in detail. Pharmacists can refuse to supply the medication. Ultimately the purchaser (or, in the case of a child, the legal guardian) is responsible for the medicine being taken according to the accompanying label; the pharmacist may simply remind them to do just that.

There are opportunities for greater involvement of pharmacists in patient care. For example, a register of patients advised by the pharmacists could be set up in each pharmacy and any purchase of antibiotic be notified to the patient's GP. The Working Party recognized the major difficulties in implementing these proposals. The lack of a unique identifier before the advent of the NHS number is a serious handicap. A simple solution using information technology (IT) will be essential in order to avoid significant administrative overheads. A robust system for notifying adverse reactions (especially allergies) should be explored which should be notified to GPs so as to maintain a complete health record (i.e. the GP should remain the single point of reference even if the patient visits multiple pharmacies).

Consensus view. There are significant problems under the present retail arrangements which prevent pharmacists from playing a greater professional role in advising and monitoring the public in relation to any increased use of antibacterials for self-administration. We would also like to see systems in place to improve communication between pharmacists and doctors so that the health record maintained by the GP is as complete as possible. This will probably be impracticable before improvements are made in IT, such as a 'smart card' with the individual's NHS number and indeed the introduction of the new NHS number. Progress with the continuing introduction of new self-medication products should not necessarily be delayed for this.

Assessing the impact of regulatory change

Safety. At present there is no system for systematically collecting data on the safety of drugs used by self-medication by either P or GSL status, although there are several routes by which information on adverse events may be reported to the MA holder and the MCA. There may be a case for improving the collection of data on adverse events, perhaps by systematic sampling, but we see no differences in this respect between antimicrobials and other medicines and those taken on prescription or by self-medication.

Impact on ecology of resistance. If selected antimicrobials are made available for self-medication, then some monitor-

ing of the impact this may have on the ecology of pathogenic microbes is desirable. Health professionals and drug regulatory authorities have a duty to protect the public from the harmful effects of medicines which might arguably extend to preventing, as far as possible, increases in antibacterial resistance. To do this it is important to collect data on both antibacterial use and bacterial resistance. Presently many of the data on resistance have deficiencies for the reasons given above. All those problems apply with equal force to antibacterials available only on prescription. It is also important to realize that the level of resistance among pathogens to a POM antibacterial has not yet led to the withdrawal of licences for the indication in question.

While there are difficulties with regard to microbiological testing in the self-medicating population obtaining medicines from pharmacies, many patients will still attend their GP and present opportunities for assessment. Therefore some possibilities to collect ecological impact data might be as follows.

- (1) Testing of all first-time presentations with the indication in question to 'spotter' practices to ascertain whether the pattern of pathogens and resistance to antimicrobials changes with time when an antimicrobial is available for self-medication. Such studies would need to be properly funded, follow agreed protocols and return data to an overseeing organization.
- (2) Testing of patients attending their GP with relapses of symptoms and comparing those who have or have not self-medicated. Similar caveats apply, as above.
- (3) Comparing the profiles of pathogens and resistance patterns in areas where self-medication is low (e.g. in practices where almost all patients receive free prescriptions) with those where self-medication is likely to be greater (e.g. practices in relatively affluent areas). PACT data for prescription use would also need to be considered.

Each of these approaches has significant deficiencies since it would be difficult to be certain that patients attending their GP constitute a population the same as those attending pharmacies for the purchase of self-medication. Thought should be given as to how pathogens for the latter population could be studied. An organization like the BSAC is well placed to develop recommendations in conjunction with industry and regulatory agencies to develop robust proposals that could form the basis of a more satisfactory monitoring arrangement for antibiotic resistance.

The promoter(s) of the antibacterial for self-medication should bear the cost of surveillance studies specific to that agent. Such data would support applications for licensing and any subsequent changes in the UK and other countries. If this is the case it is desirable that standardized and internationally acceptable methods of susceptibility testing be used.

There is no point in setting up surveillance systems

without an agreed strategy for dealing with the data which are collected. This should include a predetermined increase in resistance which must trigger a review of the licensing of OTC antibacterials. These data would be part of a package which would be presented at review of the licence renewal; and would require professional advice on interpreting such data.

Consensus view. Before and following the introduction of an antibacterial for self-medication surveillance of the impact on resistance is desirable together with agreed targets which should prompt review of OTC availability. It is recognized that there are formidable challenges with regard to the logistics and the interpretation of the data but these should not be used as an excuse for deregulation without proper surveillance

Special studies prior to P-status licence

In the USA the GSL-equivalent licensing authority requests that 'actual use' studies are done to establish that patients can self-diagnose and use the medication properly. Usage studies typically evaluate the appropriateness and adequacy of labelling (including legibility, comprehensibility, interpretability and intent-to-act) for the purchaser, compliance, off-label usage, overdose potential (especially in children) and safety issues. Actual use studies do not address pharmacodynamic or pharmacokinetic characteristics of the drug since these will have been addressed during the original licence application. Currently there would seem to be legal difficulties with regard to doing such trials in the UK with POM drugs. Occasional trials of this type may be useful for testing symptom recognition by users in relation to target indications, and due consideration might be given to modifying the law so that they can be done. Guidelines have been proposed in the EU requiring consumer testing of PILs to ensure that people understand the indication for self-medication and the proper use of the drug.³⁴ Writers of PILs should also consider using the 'Crystal Mark' scheme (see the Plain English Campaign website at <http://www.plainenglish.co.uk>).

Advertising

Advertising of P-status medicines to the general public is permitted, unlike POMs which can only be advertised to health professionals. Indeed, it would seem to be desirable if the public is to be informed of the existence of a medicine appropriate for self-medication in treating particular infections. Furthermore, no company would go to the expense of seeking a POM-to-P switch if it were not permitted to maximize its income through ethical advertising. There are clearly concerns that advertising may lead to unwarranted or inappropriate use. Advertisements and promotional activities must therefore observe the agreed code of practice which responsibly emphasizes that self-medication

must *only* be used for the stated indication. Without this 'indication drift' might occur.

Advertising is covered by a Code of Standards (issued by the Proprietary Association of Great Britain), which has a regulatory framework.³⁵

Declarations of interest

Professor D. S. Reeves is a consultant to Johnson & Johnson MSD Consumer Pharmaceuticals, Europe. Professor R. G. Finch is a consultant to Nexstar, GlaxoWellcome, SmithKline Beecham Pharmaceuticals and Bristol-Myers Squibb Pharmaceuticals. Professor A. Li Wan Po has acted as a consultant to Boots Healthcare International and Novartis.

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Over-the-counter antibacterials

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