



**BRITISH GENERIC MANUFACTURERS ASSOCIATION**

**Response by the  
British Generic Manufacturers Association  
(BGMA) to the  
DG Competition Pharmaceutical Sector Inquiry  
Preliminary Report**

The British Generic Manufacturers Association represents the interests of UK-based manufacturers and suppliers of generic medicines and promotes the development and understanding of the generic medicines industry in the United Kingdom

Generic medicines contain the same active ingredient and are as effective as the equivalent brand and cost much less, making the NHS drugs bill affordable. 64% of all medicines dispensed by the NHS are generics yet they cost only 29% of the NHS drugs bill, a saving of around £7.5bn in England & Wales alone. Without generics, the NHS drugs bill would be approximately twice its current level. The average cost to the NHS of a generic medicine is £4.62, whilst the average cost of a branded medicine is £20. Competition from generics also stimulates the research based pharmaceutical industry to develop new medicines

Our 19 members account for around 85% of the UK generics market by volume. Their work keeps medicines affordable for the Department of Health which allows further investment in other healthcare priorities, and promotes innovation in the development of new medicines

## Summary

The BGMA, representing manufacturers and suppliers of generic medicines at the manufacturing level in the UK, welcomes the Preliminary Report of DG Competition's Pharmaceutical Sector Inquiry. The Report's findings confirm the BGMA's experience of the activities of the originator pharmaceutical sector in their attempts to delay or prevent the launch of generic medicines.

At Annex is a submission to the UK Parliament's Health Select Committee made in August 2004 which lists a number of these activities, and estimates their cost to payers—in the UK, the National Health Service (NHS). Though some of the activities mentioned in our earlier report have subsequently been prevented by legislative and regulatory change—notably the Commission's 2001 Pharma Review—DG Competition's Preliminary Report shows that others continue.

We strongly support action by the European Commission to prevent or deter the continued use of the "tool box" of strategies employed by the originator sector to prevent or delay generic competition by:

- Taking enforcement action where the actions of the originator companies break competition law.
- Proposing legislative or regulatory change where originators' actions do not break the law but where they act against public policy objectives which properly reflect the interests of citizens.

## The public policy background

As we said to the UK Parliament in 2004, European and UK national legislation and regulation in the pharmaceutical field has the twin objectives of (1) ensuring public safety through regulation and (2) promoting an industrial policy for pharmaceuticals that ensures that citizens are able to receive effective, high quality medicines at an affordable cost.

Within this latter objective, generic medicines play an essential role by:

- Providing low-cost high-quality versions of older medicines once the patent protection on those products lapses, thus reducing the medicines bill and allowing the NHS to pay higher prices for newer branded medicines, ensuring that originator pharmaceutical companies have the funds to research and develop truly new innovative products (the "headroom" principle).
- Providing competition for older medicines produced by originator pharmaceutical companies, thus offering a commercial impetus for them to research truly innovative new chemical entities against which generic medicines cannot compete during the period of patent protection.

Where the activities of originator companies prevent the generic medicines industry from fulfilling these roles, the results are that:

- Payers—the NHS in the UK but, irrespective of the mechanism, citizens in one way or another—pay more for medicines, thus reducing their true availability to citizens and the money available to support true research and innovation.
- There is less innovation, denying citizens the development of truly new medicines and treatments that society needs.

Indeed, it could be argued that, by diverting their resources from their core role of innovation to efforts to delay or prevent generic competition, originator companies are not just acting in a way that is contrary to established industrial and social policy for the sector at European and national levels, they are flying in the face of the very principles that underpin that policy established by, amongst other policy makers, former Commissioner Martin Bangemann during the pharmaceutical round tables that he established.

It is against the interests of citizens and national concerns for the originator sector to act in this way. Not only do they divert resources from true research and innovation to countering generic competition which would otherwise incentivise them to develop new products, they also claim that generic competition is damaging their business model and seek further intellectual property protection and other government or official support.

This is wrong minded. Generic competition drives innovation. Originators often support their calls for more protection by arguing that more new chemical entities are now developed in the US than the EU. They ignore in these arguments that the originator sector enjoys lower levels of intellectual property and similar protection in the US than in the EU. For example, in the US, patent term extension extends to 14 years; in the EU, to 15 years; data exclusivity is at 5+3 years in the US: and 8+2 years in the EU.

Generic competition drives innovation. The activities of the originators to delay or avoid that competition damages the generic industry, citizens (and others) who pay for medicines, and innovation itself. Through enforcement action and necessary legislative and regulatory change, it is crucial that the Commission ensures that the operation of the market reverts to what was intended: that originators receive long periods of market monopoly on their products during the patent term so that they can recoup their research investment, followed by the immediate onset of generic competition to make medicines affordable and to promote true innovation.

## Priorities

DG Competition's report identified a tool box of strategies employed by originator companies to delay or prevent the onset of generic competition. In the context of the UK<sup>1</sup>, we see the most important strategies being (most important first):

1. Evergreening, including vexatious legal challenge around weak patents, often supported by inaccurate information campaigns about the bioequivalence of generic medicines and their safety, quality and efficacy.
2. The inadequate application of patent law by intellectual property authorities (the EPO and national agencies) and the Courts in tandem with spurious threats to potential entrants to the market.
3. Interference with the MHRA<sup>2</sup> in the grant of marketing authorisations<sup>3</sup>.

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<sup>1</sup> A predominantly INN market with high levels of INN prescribing (>80%) for all products irrespective of patent status and without the need to apply for separate reimbursement or currently substitution status. [Note that the UK Government is currently consulting on the introduction of generic substitution, so this may change.]

<sup>2</sup> The UK marketing authorisation agency—the Medicines and Healthcare Products Regulatory Agency.

<sup>3</sup> Note that there is no separate granting of pricing and reimbursement status for generic medicines in the UK, which explains why the EGA (European Generic medicines Association) and other EU generic industry representatives may see this as a higher priority.

We comment on these below. In addition, as DG Competition's report recognizes, the generic industry faces barriers to market entry due to bottlenecks in the procedures for the granting of marketing authorizations and variations. We also comment on this issue.

## Evergreening

### Second generation products

A key strategy adopted by originators, and identified in our 2004 submission to the UK Parliament's Health Select Committee (at Annex), is that of originators developing second generation products, based on the original, often with little or no additional therapeutic benefit to patients. They then withdraw the original shortly before patent expiry, and encourage medical General Practitioners (GPs) to prescribe the second generation product instead of the first.

There are different variations on this theme:

1. Originators may simply withdraw the initial product shortly before patent expiry, and replace with the second generation product. That change itself, but supported by marketing campaigns to GPs, results in their changing their prescribing habits to the second generation product. Even where the degree of change is such that there are no patents on the second product, however weak, this acts as a barrier to generic market entry. The market for the initial product is killed—if a medicine is no longer prescribed, there is *de facto* no market for it. It will then typically take a generic company a further two to five years to develop, register and launch the equivalent generic.
2. The delay will be exacerbated if the originator succeeds in gaining a patent on the second generation product. We explore below the difficulties faced by generic companies in launching legal challenges even to weak patents.
3. Minor changes to the initial product—such as the use of different salts or form—can create a barrier to generic market entry if the switch to the second generation product is effected through changes to GPs' prescribing software which favours the second generation product. The software suppliers in the UK tend to use data from the first SPC<sup>4</sup>, ie, that filed by the originator, or data supplied by the originator. This can offer a significant barrier to generic market entry if, as has been the case, this results in computer generated prescriptions defaulting to the second generation formulation or form, eg INN + specific salt or form. In these circumstances, only the second generation brand could be dispensed even though the GP may believe that he or she had prescribed a generic by virtue of the INN.
4. Originators may offer GP practices help to "tidy up" their prescribing computers, and use this as an opportunity, for example, to change patients receiving repeat prescriptions to the second generation or revised form of the product. Though a GP's authority is required for this change to be made, this may often be given without the GP having a full understanding of the consequences of giving his authority and where the implementation of change is delegated to be carried out in a mechanistic fashion across all patients.
5. Originators may make false or misleading claims to GPs and others about the supposed clinical benefit of the second generation product, or about the comparative safety, quality and efficacy of the generic version of the initial product. This may lead to GPs taking their prescribing decisions on the basis of false or misleading information.

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<sup>4</sup> Summary of Product Characteristics.

None of this is to say that the BGMA is opposed to continuous development of medicines, or incremental innovation. Some of our members invest in incremental innovation, for example by the development of specific delivery systems or paediatric liquid forms of well established solid dose products. These developments clearly have clinical and other patient benefit, sometimes to the extent that these developments are sufficiently inventive that they may be granted a patent.

However, we strongly object when GPs are prevented from exercising their discretion to prescribe the initial or second generation product having reached a view on whether the inevitable additional cost of the second generation product is justified by the clinical benefit, if any. If GPs are denied this choice, either by these actions delaying or preventing generic launch, or because the true facts of the case are hidden from or misrepresented to them, then we believe these activities are anti-competitive and we would urge the competition authorities to take enforcement action.

## Vexatious legal challenge

Under current arrangements, the balance of risk between originator and generic companies is such that originators may often decide to threaten or bring legal action against generic companies typically for breach of patent even when they know that their case is weak. This is particularly egregious when the legal action is accompanied by an application for an interim injunction to prevent launch of the generic.

In many cases, generic manufacturers are small or medium sized enterprises (SMEs). They have neither the financial nor human resources to mount a sustained legal defence against a case brought by a multi-national business. This may particularly be the case where, as identified in the Preliminary Report, originators create patent "thickets" around a product: the Report referred to 1300 patents in the case of one product<sup>5</sup>. An SME will simply not have the resource to find its way through this sort of legal thicket and will often find it commercially more secure to withdraw from the planned product launch, even though we note that the Inquiry found that the majority of cases that go to Court are found in favour of the generic company. Frequently, they cannot afford to bear the potential costs of losing a case, particularly where they may have to bear the costs of the originator as well as their own.

We do not, of course, object to the right of any entity to seek recourse to the courts to uphold their rights. However, we believe that the Preliminary Report and our own experience provide powerful evidence that the creation of patent thickets and the uncertainty that they pose to generic companies are often part of comprehensive strategies employed by originators to deter or delay generic market entry. These actions under these circumstances may be anti-competitive and, where they are, we urge the authorities to take enforcement action.

As the Commission found, originator companies frequently seek interim injunctions to prevent the marketing of generics pending the outcome of a legal challenge. This has the effect of ensuring that the originator continues to receive the full revenue from the use of the product at least until the case is resolved. Should the originator win, they may receive costs

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<sup>5</sup> We noted Lord Justice Jacob's comments at the Commission's presentation of its Preliminary Report that other sectors, such as mobile telephones, attracted greater numbers of patents around specific products and that, thus, this concern was unjustified. We find this comment irrelevant and wrong minded. Bluntly, the lack of access to a mobile telephone does not, of itself, put at risk the health and lives of citizens: the lack of access to affordable medicines does. The law does not sit in isolation. It is the legislator's means of giving effect to agreed public policies. If it fails properly to implement those policies, it needs more rigorous enforcement or to be changed. It is clear in this case that the creation of patent thickets is used on occasion to frustrate the launch of generic competition. Thus it may be anti-competitive, and clearly does show evidence of a failure of the legislation or its enforcement to meet agreed public policy imperatives.

awarded against the generic company. Should the generic win, they may receive compensation for their lost revenues.

But the disparity in prices of the original brand and the generic are such that the originator company will have more than covered its costs by the revenues gained during the period of injunction. The real losers under these circumstances are the payers—in the UK, the NHS. Under these circumstances, the NHS normally bears the additional prices it is forced to pay during the period of the injunction. Apart from the obvious loss to the public purse and consequently to citizens, these arrangements mean that the balance of risk in these actions is overwhelmingly in favour of the originator.

We submit that it is wrong that originators should be able to act in this way without risk, and that their actions are effectively underwritten by citizens. We believe that the balance of risk between originator and generic should be more balanced, and (in the UK's case) the NHS should be absolved from bearing the greater costs it faces. We note that, on the rare occasions that the NHS has joined legal actions of this type in the UK<sup>6</sup>, originators have tended to withdraw the action because of the balancing of risk. We believe that, when costs are awarded in cases such as these, they should always include the costs suffered by the payer both in fairness and to balance the risk faced by originator and generic companies.

## Inaccurate information campaigns

From time to time, we have been aware of specific campaigns aimed at undermining the use of generic or biosimilar medicines based on the communication of inaccurate or incomplete information. Examples include:

1. An originator company writing to all Primary Care Trusts (PCTs<sup>7</sup>) alleging that generic versions of a particular product were not the same as the originator product, even though the allegation had been specifically considered by the EMEA and rejected.
2. A biopharmaceutical company organising a meeting in the UK Parliament at which experts it had selected answered questions posed by Members of both Houses, again selected by the sponsoring company. The company subsequently published a report of this event, which it characterised as a "Parliamentary report".

None of these allegations can have a basis in fact since all generic and biosimilar medicines are shown to be bioequivalent as part of the approval process. It may be possible for the competition authorities to take enforcement action in some cases, and we would welcome this. In addition, the Commission should propose a legal prohibition on the use of negative information in marketing campaigns.

## Inadequate application of patent law

The inadequate application of patent law can prevent the operation of a truly competitive pharmaceutical market when:

1. Patents are too easily issued by the EPO or national patent authorities when the applications do not properly meet the appropriate tests for approval.
2. Courts support weak or invalid patents so issued due to a lack of technical skill and understanding.

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<sup>6</sup> eg, Generics (UK) and others v Abbott Laboratories (2004).

<sup>7</sup> PCTs are responsible for prescribing budgets and advise their GPs on appropriate prescribing practice.

## Patent approval

We believe that competition law may be breached when an originator makes applications for patents which it knows, or ought reasonably to know, should not be granted; or where it deliberately withholds evidence from the examiner that it knows, or ought reasonably to know, is relevant to the application and may result in it not being granted.

But competition law will not, of itself, resolve all of the problems associated with the granting of weak patents and their proliferation. It is simply too easy to obtain weak patents through the EPO and national patent agencies. Action should be taken to “raise the bar” in terms of the quality and thoroughness of the assessment of patent applications. This should not be taken to imply that we necessarily seek a change in the fundamental rules: rather, we seek to avoid poor decisions brought about by the lack of time and information available to the examiner.

Specifically, we propose that:

1. There should be a more rigorous assessment of patentability requirements, particularly the application of the inventive step requirement.
2. Applications for divisional patents should not cover essentially the same subject matter as the parent application.
3. Resources should be made available to allow more rigorous assessment.
4. Applicants should be under a “duty of candour” requiring them to disclose with their applications all relevant information known to them.

## Patent litigation

It is equally important that cases brought before the Courts apply a similarly rigorous test of what is patentable. Recent experience in the UK suggests that the Courts may be applying a lower hurdle to the test of patentability, again particularly around the issue of obviousness and the inventive step.

The Report suggests that structural issues related to patent litigation in the EU may be best addressed via the introduction of a Community patent and a unified judiciary. The success of this approach would depend upon the details; but the creation of a specialised and expert unified judiciary are key. This would need to provide that:

1. In all jurisdictions, patent cases would be handled by specialised patent judges with the necessary technical knowledge and expertise to decide cases quickly and correctly.
2. The current over-readiness of certain jurisdictions to grant interim injunctions excluding generic medicines from the market should be reversed (the introduction of expert specialist judges might be a significant help in this regard).

If many of the problems referred to in the Preliminary Report are to be dealt with, it is essential that change is made which brings about the creation of expert judges and reverses the current over-use of interim injunctions.

## Interference in the grant of marketing authorisations

There has been relatively little direct interference by originators in the determination of marketing authorisation applications by the MHRA. We do, however, have experience of originators:

1. Alerting the MHRA to potential safety related issues in a product shortly before patent expiry with the apparent intention of delaying generic launch.
2. Seeking to make presentations to the MHRA's expert advisory committees, possibly to raise unfounded doubts in their minds about the safety of a particular category of products.
3. Using freedom of information legislation to mount a fishing trip to discover which generic companies had made marketing authorisation applications prior to patent expiry<sup>8</sup>.

We believe that, where it can be shown that an originator's actions in this way are part of a plan to delay generic competition, the competition authorities should take enforcement action. There may also be a case for legislative change limiting the ability of originators to interfere in marketing authorisation processes.

## Regulatory delays

In addition to the actions of originators to prevent generic market entry, delays to generic launch may be caused by slow or late authorisations which have to be granted by the relevant authorities<sup>9</sup>. In the UK, this has been due to:

1. Inadequate numbers of assessors and inaccurate predictions of workload, or lack of appropriate efficiency levels.
2. Creation of new regulatory hurdles or burdens<sup>10</sup> without appropriate lead time or recruitment of additional assessors.
3. The unwillingness of many European agencies to act as reference Member State in the decentralised procedure, leaving a small number of agencies, including the MHRA, to shoulder the burden.
4. Other interference with regulatory mechanisms for establishing generic names and pharmacopoeial standards for products with multiple ingredients.

## Conclusion

We hope that the European Commission finds this submission helpful. We should be delighted to answer any further questions on it.

**Friday, 30 January 2009**

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<sup>8</sup> In this case, the MHRA erroneously gave the originator the data it had sought in contravention of its own procedures on commercial confidentiality. We discovered the breach only when the MHRA wrote to the companies concerned to apologise.

<sup>9</sup> In the UK, this is restricted to the granting of marketing authorisations by the MHRA. There are no separate processes for pricing & reimbursement or substitutability approval.

<sup>10</sup> eg User testing of Patient Information Leaflets.

# Annex: BGMA Submission of 16 August 2004 to the UK Parliament's Health Select Committee Inquiry into the Influence of the Pharmaceutical Industry

## Health Select Committee Inquiry The Influence of the Pharmaceutical Industry

Memorandum by the British Generic Manufacturers Association (BGMA)

### Summary

1. The role of the generic pharmaceutical industry within the NHS is:
  - To provide low-cost high-quality versions of older medicines once the patent protection on those products lapses, thus reducing the medicines bill and allowing the NHS to pay higher prices for branded medicines, ensuring that originator pharmaceutical companies have the funds to research and develop truly new innovative products (the "headroom" principle).
  - To provide competition for older medicines produced by originator pharmaceutical companies, thus offering a commercial impetus for them to research truly innovative new chemical entities against which generic medicines cannot compete during the period of patent protection.
2. These principles have been adopted and endorsed both by the European Commission, and the UK Government. However, the launch of generic equivalents to branded products does not always take place immediately following expiry of the patent protection enjoyed by the brand. In some cases, this may be due to technical or scientific issues.
3. In others, however, it can be due to a failure of the policy and legislative framework within which the generic pharmaceutical industry must rightly operate, and this failure may be subject to influence exerted by the originator branded pharmaceutical industry. Clearly, if originators are able to delay the launch of generic versions of their products, they extend the commercial life of them.
4. We believe that the Government should be more alert to activity undertaken to produce this "evergreening", and act in a more concerted and joined up way to prevent it happening. Only in that way will the Government ensure that the NHS fully benefits from the reduction in the prices of medicines brought about by generic competition.

### The British Generic Manufacturers Association (BGMA)

5. The BGMA is the representative trade body of the manufacturers and suppliers of generic medicines in the United Kingdom. Our members are: APS / Berk (Teva), Alpharma, Crescent Pharma, Dr Reddy's Laboratories, Generics UK (Merck), Genus

Pharmaceuticals (Stada), IVAX, Kent Pharmaceuticals, Ranbaxy, ratiopharm, Rosemont, Sandoz and Sterwin (Sanofi).

6. We believe that our membership accounts for more than 80% of the supply of generic medicines in the UK.

## Generic medicines

7. A generic medicine is one that contains the same active ingredient as an original branded product. It is subject to the same regulatory standards of safety, quality and efficacy as the original brand; and, before being marketed in the UK, must similarly receive a marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA).
8. However, rather than having unnecessarily to reproduce data relating to preclinical and clinical trials as with an originator product, a generic manufacturer instead needs to demonstrate that the generic product is essentially similar to the original brand in terms of its effect on the patient. This not only avoids the need for unnecessary trials on animals and humans, but reduces the research and development costs involved in bringing a generic medicine to the marketplace.
9. Under current UK legislation<sup>11</sup>, a generic manufacturer may make a so-called abridged application for a marketing authorisation to the MHRA, based on demonstrating “essential similarity”, ten years after the commercial launch of the original product<sup>12</sup>. Once the MHRA has issued a marketing authorisation, the generic medicine may be launched, so long as any relevant patents on the original brand have expired. It may take two years or more to develop a generic version of an original brand.
10. Thus, after the expiry of the patent or patents covering an original branded medicine, there are a number of versions of that medicine in the marketplace: the original brand, and any number of generics, depending upon the number of generic manufacturers that chose to launch the product. Under a community pharmacist’s terms of service, the pharmacist must dispense the brand if the GP writes a prescription for the brand; but a prescription written generically may be met by the generic or the brand (since the two are equivalent and thus interchangeable). In the latter case, however, the community pharmacist is reimbursed at the lower generic price, even if the brand is dispensed.
11. The reimbursement price of a branded medicine under the NHS is directly related, and can be close to its market price. Market prices are only indirectly regulated by the Department of Health under the Pharmaceutical Pricing Regulation Scheme (PPRS), which sets a limit on the overall profit that members of the Scheme are able to make. The PPRS takes account of the very significant research costs borne by the branded sector and also provides allowances for promotional and advertising activities.

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<sup>11</sup> Changes to the detail but not the principle are due to be implemented next year.

<sup>12</sup> It is open to a generic manufacturer to make a different form of application before the expiry of this ten-year period of “data exclusivity” by undertaking its own preclinical and clinical trials; but an abridged application under which the MHRA compares the similarity of the generic with the data submitted by the brand originator in support of its application is the normal way of bringing a generic to the market.

12. Because there are typically a number of suppliers of most generic medicines, the market price paid by community pharmacists and wholesalers is set by competition between generic manufacturers. Different generic manufacturers compete largely, but not wholly, on the basis of the price of their products<sup>13</sup>. The reimbursement price paid to community pharmacists by the NHS (the Drug Tariff price) is determined on a monthly basis by the Department of Health and is based upon a weighted average of the list prices of five suppliers (three generic manufacturers and two wholesalers, the latter contribution being weighted double: ie, manufacturers provide three sevenths of the prices taken into account, and wholesalers four sevenths).
13. Competition naturally drives down prices and, according to the latest published Department of Health statistics, generic medicines account for 55% of prescriptions dispensed, at a cost of only 24% of the drugs budget. On this basis, if there were no generics available, and all medicines paid for by the NHS were priced at the average cost of brands today, the drugs bill would increase by over £5 billion.
14. [In fact, we believe that the savings due to generics could be significantly greater than this because the current reimbursement price does not fully reflect discounts from list prices that are offered by generic manufacturers. With others, we have been working with the Department of Health to agree a more realistic reimbursement scheme which will ensure that the NHS fully benefits from the savings due to generic medicines.]

## Delay in the launch of generics

15. It is clear, therefore, that any delay in the launch of a new generic after expiry of the patent or patents on an original brand is potentially very expensive for the NHS. We set out below some recent examples of where delay has been caused, at least in part due to the influence or actions of the originator branded pharmaceutical industry.
16. In many cases, the delay is due to the brand originator changing the active ingredient, formulation or pharmaceutical form shortly before patent expiry. Generic manufacturers will already be well down the road of developing generic versions of the original product. Launch of the changed version of the brand often leads to GPs prescribing the new version – particularly if the originator has withdrawn the first version from the market – and thus there is no market for the generic under development.
17. Developing the revised version may take another two years or more, delaying generic launch by that period. Alternatively, the brand originator may claim data exclusivity on the revised form, delaying generic launch by 10 years (though the recently adopted revised EU pharmaceutical legislation limits the scope for this in future)<sup>14</sup>.
18. In making these points, we must make clear that we do not seek to undermine the legitimate rights of the originator sector, nor criticise them for making the most of available opportunities to extend the commercial life of their products, especially where real benefits are given to patients and are cost-effective. However, it is crucial for everyone concerned in the NHS, not least patients, that the creative energies of the

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<sup>13</sup> Other competitive factors include quality of service, range of products available, customer loyalty schemes, etc.

<sup>14</sup> See footnote 2 for an explanation of "data exclusivity".

originator pharmaceutical companies are directed to researching and developing new medicines, which will become generic medicines in due time, rather than working to extend the commercial life of their older products and reducing the headroom created to pay for true innovation.

#### Chiral switching (Example: Omeprazole/Esomeprazole)

19. Most commonly used drugs are administered as 50:50 mixtures (also known as racemic) of enantiomers, a type of optical or stereoisomers. These are left-handed and right-handed 3-D forms of the same molecule. The originator company usually first markets its product as a racemic mixture.
20. With a view to evergreening or extending the return on the originator product and delaying generic competition, it has become a common strategy for originator companies to develop and market different mixtures of, or single isomer forms of the original product, and gain extra patent and other intellectual property protection on the new product. These invariably have no or only marginal therapeutic benefit to patients over the first originator product. Where these new products are introduced, changes to prescribing habits are promoted further restricting the market for the previously available form.
21. In this case, the originator sought to establish a distinct identity for the single isomer version by obtaining a marketing authorisation for it to be used at twice the strength of the original product (40mg for indications where 20mg was traditionally used and 20 mg where 10mg was used).
22. Marketing to GPs to prescribe the single isomer version undermined the market for generic versions of the original form which had been developed ready for launch.
23. Issues surrounding the introduction of esomeprazole are currently the subject of a competition inquiry by the European Commission.

#### Switching to active metabolite (Example: Loratadine)

24. Originators can also switch the active metabolite, potentially to the more active isomer.
25. The withdrawal of loratadine and its replacement with desloratadine prior to patent expiry similarly meant that there was no market for generic loratadine once it became available since GPs had changed to prescribing the new form, desloratadine.

#### Different formulations (Examples: Doxazosin and Mirtazapine)

26. In this case, different formulations are marketed, usually based on sustained release technologies. Historically, they were marketed alongside the original brand but increasingly they are replacing the original product.
27. Just before patent expiry the originator marketed a sustained release version of doxazosin and discontinued the corresponding strength of the conventional product.
28. Just before patent expiry the originator marketed a soluble version of Mirtazapine (Soltab) and discontinued their tablet form.

29. In each case, prescribing patterns changed so that there was a reduced market for the generic.

#### Different presentations (Example: Ramipril)

30. Ramipril was licensed and sold in the UK as a capsule. Elsewhere in Europe, it was presented as a tablet. The patent expired on 9 January 2004, at which point generic manufacturers were ready to launch Ramipril capsules.
31. The originator attempted to withdraw the capsule form in the UK, intending to replace it with the tablet form, to be sold at the same price as the capsule. The originator contacted all major wholesalers and retail suppliers informing them that capsules would be replaced by tablets with effect from 3 November 2004. A large number of GP prescribing computer systems were also changed to list and print prescriptions for the tablet form and not for capsules. Pharmacists would be required to dispense tablets if that form was specified on the prescription.
32. If action had not been taken there would have been very little or no market for Ramipril in the capsule form, when patent expiry took place in January 2004, if the majority of prescriptions had required the tablet to be dispensed. It would have taken generic manufacturers two or three years to undertake from scratch the development work for the tablet form, and gain authorisation from the MHRA.

#### Different salts (Example: Amlodipine)

33. Medicinally active chemical entities are commonly insoluble in water and are therefore manufactured in salt form to increase solubility. One of the decisions of the recent European Pharmaceutical Review was that a generic may be based upon a different salt than that of the brand if the products can be shown to have the same safety and efficacy profile. This is logical given that it is the medicinally active chemical entity that provides therapeutic benefit to patients.
34. The Amlodipine base is not water soluble, and must therefore be manufactured in salt form. The brand is manufactured as amlodipine besilate. Other salt forms include amlodipine maleate and amlodipine mesilate. Generic versions are based upon these latter two salts since, although the patent on the amlodipine base expired on 7 March 2004, there is a further patent on amlodipine besilate which does not expire until 25 March 2007.
35. The originator company wrote to GPs, in March 2004, advising that alternative salt forms were not identical to the brand (amlodipine besilate), despite the European Medicines Evaluation Agency having confirmed that the two salts were equivalent in adjudicating upon two arbitrations. In parallel, many of the GP prescribing software packages automatically produced apparently "generic" prescriptions for amlodipine besilate (ie, the brand) due to the generic description entered in the product's Summary of Product Characteristics by the originator.
36. We are still working to ensure that GPs' software produces a generic descriptor when desired by the GP that is salt neutral and allows all forms of amlodipine to be supplied by a pharmacist.

## Costs of delays

37. We have calculated below the potential cost over one year to the NHS should these circumstances lead to a delay in the onset of generic competition. In doing so, we have used two hypotheses: first, that the generic would take 50% of the market, and reduce market prices by 50%; and, secondly, that the generic would take 75% of the market and reduce market prices by 75% (the latter being more normal).

### Potential costs of delays (£ million)

<b>Product name</b>	<b>Market value before patent expiry</b>	<b>50% becomes generic and 50% price drop</b>	<b>NHS annual saving</b>	<b>75% becomes generic and 75% price drop</b>	<b>NHS annual saving</b>
Amlodipine	£185m	£139m	<b>£46m</b>	£81m	<b>£104m</b>
Doxazosin	£104m	£78m	<b>£26m</b>	£46m	<b>£59m</b>
Loratadine	£31m	£24m	<b>£8m</b>	£14m	<b>£18m</b>
Mirtazipine	£29m	£22m	<b>£7m</b>	£13m	<b>£16m</b>
Omeprazole	£181m	£136m	<b>£45m</b>	£79m	<b>£102m</b>
Ramipril	£125m	£94m	<b>£31m</b>	£55m	<b>£70m</b>
<b>Total</b>	<b>£655m</b>	<b>£492m</b>	<b>£164m</b>	<b>£287m</b>	<b>£369m</b>

## Patent law

38. The generic industry is facing growing difficulties in launching new products due to the increasing number of patents on very minor or marginal changes to pharmaceutical products. There is evidence that this could become the principal obstacle facing the industry. As an example, in the year 2000, the US Patent Office granted 6730 pharmaceutical patents whilst the US Food and Drug Administration only registered 27 new chemical entities.

39. This growing global trend has the effect of delaying the entry of new generic products, and allows the originator industry to reap continuing benefit from its older products. This not only keeps the cost of medicines unnecessary high, but reduces the incentive on the originator sector to develop truly innovative new chemical entities.

40. We believe that more should be done to simplify current patent structures, and to ensure that the growing trend of establishing numerous patents on superfluous aspects of medicines for the sake of prolonging market exclusivity should not be allowed to become common practice in the UK and the EU. This is particularly important in the light of the newly adopted EU legislation on the enforcement of intellectual property protection.

## Brand equalisation

41. We are also concerned about the way in which branded and generic medicines are treated under the Government's approach to reimbursement. This allows the branded sector to use the flexibility it enjoys under the PPRS to compete with generics in the post-

patent market in a way that is unfair and which lessens the cost savings that the NHS would otherwise enjoy as a result of generic competition.

42. Under so-called "brand equalisation", the brand originator sells a proportion of his product at the generic market price, thus allowing pharmacists to dispense a branded product against a prescription written and reimbursed generically without suffering any commercial disadvantage. Branded companies may similarly be able to "balance" prices across their patented and non-patented portfolio to gain a greater market share in segments of the market where they face the greatest competition, such as primary care. Notwithstanding the restrictions placed on modulation in the current PPRS, branded companies are able to manage the pricing of the portfolios in this way.
43. We believe that this form of competition acts against the interests of the taxpayer and patients, as well as those of the generic pharmaceutical industry. At a time when the Government intends to change the way in which generic medicines are reimbursed, we believe that it is crucial to ensure that the current competitive balance between true generics and off-patent brands is not tilted in favour of brands.
44. Indeed, we believe that it is essential that the Government ensures that the impact on this competition is properly assessed in the light of its proposals to amend the generic reimbursement scheme, and as part of its consideration of changes to the PPRS. This is apparently not being done.
45. We believe that the current scope of PPRS does not reflect the operation of the marketplace, and is thus wrong. As we have commented above, off-patent brands and generics compete in the marketplace to meet prescriptions written generically. Broadly, the PPRS applies to brands and the generic reimbursement system to generics. These are not, however, two distinct markets. Rather, there is an on-patent market and an off-patent market. The Government's schemes for managing the price of medicines to the NHS should reflect this market reality.
46. For on-patent markets, competition takes place in the doctor's surgery. Brand originator companies market their products to encourage doctors to prescribe their brand. (Even if doctors prescribe an on-patent medicine generically, only the brand will be available.) For products still under patent, therefore, there is no competition outside of the doctor's surgery: once the prescribing decision has been taken, they enjoy a monopoly in the marketplace.
47. Once a product's patent has expired, however, the scope of competition normally increases dramatically. If the product is prescribed generically, the prescription can be met by a generic medicine, typically manufactured and marketed by a number of competing companies, or by a brand. There is, therefore, usually very considerable competition at pharmacy (and wholesale) level. However, if the brand originator succeeds in persuading doctors to continue to prescribe the brand after patent expiry, no price competition exists at pharmacy or wholesale level.
48. We believe that these features of the marketplace under the current twin systems of price regulation (the PPRS and the generic pricing in the Drug Tariff) act against the interests

of the NHS and the taxpayer. We believe that the market would be more competitive and more dynamic, and more closely meet the public policy principle of “headroom”, if one form of price regulation – the PPRS or its successor – were to apply to the on-patent market, and another – the proposed revised generic reimbursement scheme – to the off-patent market.

49. We have urged the Department of Health to seek to renegotiate the PPRS along these lines.

## Conclusion

50. The Department of Health has from time to time intervened to ensure that the launch of generics, and the benefit that that brings for the NHS, is not delayed and is fully realised. That intervention has, however, been sporadic and *ad hoc*. There has, further, been little co-ordination between the different government agencies involved, and external suppliers to the NHS.
51. We believe that, if the NHS is to achieve the maximum benefit from generic competition, the Department needs to take a more holistic approach. We have raised these issues with them and are confident that they will respond positively. We should, however, very much welcome the Committee’s endorsement of this view.

**16 August 2004**

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