

# Pharmaceutical Parallel Trade in the UK



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Panos Kanavos  
Paul Holmes

Commentaries by

David Loudon  
Sue Mitchell  
David Taylor  
Jim Thomson

Benedict Irvine (editor)

First published April 2005

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77 Great Peter Street  
London SW1P 2EZ  
email: books@civitas.org.uk

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ISBN 1-903 386-39 X

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Typeset by Civitas  
in Palatino

Printed in Great Britain by  
The Cromwell Press  
Trowbridge, Wiltshire

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## ***Authors***

**Panos Kanavos**, lecturer in International Health Policy in the Department of Social Policy and Merck Fellow in Pharmaceutical Economics at LSE Health and Social Care.

**Paul Holmes**, researcher, London School of Economics.

**Benedict Irvine**, formerly Director of the Civitas Health Unit, he now works in the NHS.

**David Loudon**, Category Manager Dispensing Buying, for Boots The Chemists.

**Sue Mitchell**, Communications Manager of Epilepsy Action and Editor of *Epilepsy Today*.

**David Taylor**, Professor of Pharmaceutical and Public Health Policy, School of Pharmacy at the University of London, and an NHS trust chairman.

**Jim Thomson**, Chief Executive of Depression Alliance.

## *Foreword*

### **Parallel Trade In Pharmaceuticals: Is Patient Safety Being Threatened In The UK?**

The UK is a major parallel import destination. Parallel trade involves the legal repackaging and re-selling of genuine medicines. There are entrenched views on the subject of parallel trade in pharmaceuticals. On the one hand we have importers, who argue that they are pursuing a legitimate business in a free-trade area, making significant profits through price mark-ups. On the other hand, manufacturers see profits dented by parallel importing, and are frustrated at governmental price and reimbursement regime regulation—the primary cause of price differentials. Manufacturers and their associations argue that there is a knock-on effect on investment in the development of new drugs. Parallel traders refute this argument, and point to significant economic benefits brought to our NHS from their business; a recent study by health economists Peter West and James Mahon, funded by the European Association of Euro-Pharmaceutical Companies (EAEPC), supports this economic benefit theory.<sup>1</sup> However, an LSE study carried out by co-author of Part I of this pamphlet Panos Kanavos, found that the benefit to the NHS, and therefore patients through lower prices, was negligible.<sup>2</sup> The methodology and findings of this LSE report were fiercely criticised by the EAEPC.<sup>3</sup> Kanavos and Holmes revisit and examine the growing literature on the subject in their contribution.

However, this report is not directly concerned with these economic-benefit and R&D issues. Rather, Kanavos and Holmes set out in detail the facts on parallel trade from continental Europe to the UK. How are products brought into the country? What is the legislative framework? Are the obligations under which parallel distributors operate followed strictly?

Part II of the report offers hypotheses about only one potential spillover effect—the undermining of patient safety. Drawing on evidence from Kanavos and Holmes and various stakeholders including patient organisations, a dispensing chemist, pharmaceutical manufacturers and their representatives, the report considers whether a high volume of parallel trade gives rise to legitimate concerns about patient safety and consumer protection. Are parallel imports acceptable to patients? Is sustainability of supply a problem? Is there evidence of product tampering and incorrect patient notes? And is product recall of goods easy? If any of these concerns are genuine, how can we protect patients without erecting barriers to legal trade?

Counterfeiting is a serious risk to patient safety. There is a recent example of one such product entering the Dutch supply chain as a parallel import, but Kanavos and Holmes found only one UK example in the previous eight years.<sup>4</sup> Some patient groups believe that individual patients may be less alert to the risk of counterfeits if they are told that their medication might be an orange oval one month and a pink triangle the next, and that there is nothing to worry about if the packaging is in Greek. This reduction in alertness to risk is a valid concern and Ben Irvine considers alternative arrangements that would help to overcome the problem.

The UK market of parallel distributors is made up of 14 key companies who are members of the British Association of European Pharmaceutical Distributors (BAEPD). Although Kanavos and Holmes refer to these 14 companies, they do not examine smaller-scale traders in great depth. The majority of parallel import licences are granted to these non-BAEPD members, which suggests that the products concerned have smaller market share and are not imported in great volumes (see Table 5.10, p. 41). Further research will be necessary in order to determine exactly how many companies are involved in bringing pharmaceutical products into the UK. Such research may yield similar or more serious concerns.

Civitas is very grateful to Pfizer, Boots and the Atlas Economic Research Foundation for supporting this project

*David G. Green*

## Part I

### Pharmaceutical Parallel Trade in the UK

Panos Kanavos and Paul Holmes\*

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\* LSE Health and Social Care, London School of Economics and Political Science. The authors are grateful to two academic referees for helpful comments and suggestions in earlier drafts. All outstanding errors are the authors' own.



## ***Executive Summary***

The parallel trade in pharmaceuticals dates back to the 1970s when a number of pharmacists realised that drug prices varied significantly between member states of the EEC. To take advantage of this they established small wholesale businesses from their dispensaries, supplying other local pharmacies initially and, subsequently, the wider UK health service. In 2002, the UK market for parallel-distributed pharmaceuticals represented £1,300 million (€2,000 million) and is the largest market in the EU.

Advocates of pharmaceutical parallel trade, such as public-health authorities, maintain that it is important to be able to purchase drugs from the cheapest possible source, thus favouring an open régime for pharmaceutical parallel imports (PI). Conversely, supporters of strong international patent rights for new medicines promote a global policy of banning PI, believing that if such trade were widely allowed it would reduce profits in the research-intensive pharmaceutical sector and ultimately slow down innovation.

Pharmaceutical parallel trade has grown consistently in the European Union due to the principles of free movement of goods, the regional exhaustion of intellectual property rights<sup>1</sup>(IPR), as well as a series of European Court of Justice (ECJ) rulings. Article 28 of the EU Treaty prohibits all measures which have the equivalent quantitative effect of restricting the free movement of goods between member states, including national intellectual or industrial property rights. Exceptions to this rule fall under Article 30 and justify the protection of industrial and commercial property rights ('specific subject matter' only), the exhaustion of rights and the pursuit of public health. In addition, parallel trade is encouraged by the governments of several member states, especially in countries where overall price levels for in-patent pharmaceuticals are at or above the European average (UK, Sweden, Denmark, Germany, the Netherlands).

The conduct of parallel trade has raised several issues of legislative, regulatory, institutional, market structure, and economic nature. This paper has examined these with particular reference to the UK.

### ***A. Legislative issues***

As a result of numerous cases heard before the European Court of Justice (ECJ) since the late 1960s, a number of issues appear to have been resolved; in this context, specific policy implications of parallel trade include that:

- a) Parallel distributors do not have to repackage products, but may do so if they adhere to specific guidance, such as the protection of the condition of the product and the reputation of the trademark, giving the trademark owner notice, and stating on the product that it has been repackaged;
- b) Member states are required to afford simplified national registration rules for parallel importers such that if the health authorities of the destination country already possess the relevant information for the identical medicine, no further obligation is placed on the parallel importer;
- c) Provided the medicines are therapeutically identical, i.e. contain the same active ingredient in the same amount and same dosage form, there is no obligation for a parallel imported product to have a common origin to a domestic brand;
- d) Member states can disallow parallel imports for reasons of protecting public health and safety, including differences in product formulation and package size modifications that may mislead consumers (Article 30 of the EU Treaty);
- e) Manufacturers can manage their inventory so long as there is no outright ban on exports, no monitoring of the final destination of the product, and no agreement between undertakings (manufacturers & wholesalers);
- f) Important issues remain unresolved but are likely to be heard before the ECJ in the near future; most notably, these include (a) dual pricing, in the context of defining the

geographical boundaries of a (national) market<sup>2</sup> and (b) the abuse of dominant position<sup>3</sup> and the criteria for defining it. Two pending cases (one on dual pricing [Spain] and one on abuse of dominant position [Greece]) which will be heard by the ECJ in 2005 are likely to influence future policy direction on parallel trade, depending on the court's rulings;

- g) With ten new member states having joined the EU on 1 May 2004, it will also be necessary to observe how these will affect the future of parallel trade and how the EU will apply its governing principles, especially the principle of derogation.

### ***B. Regulatory issues***

There are few hurdles before gaining marketing authorisation of parallel-imported pharmaceuticals through the centralised and the national regulatory procedures. Testing is not needed, the product name can remain the same (although national regulatory authorities typically advise for the brand name prevailing in the member state of importation to be used), and the costs of the application are substantially lower than those of a new substance or a generic product. One key barrier to parallel importing of pharmaceuticals is the need for relabelling of the product and the insertion of a patient leaflet in the language of the destination member state. In some member states (e.g. the Netherlands), pharmacists can set up a wholesaling company and maximise their purchasing economies. The costs of obtaining a license for doing this does not appear to be a barrier.

There are regulatory controls for parallel imported pharmaceuticals in each destination country. Regulatory approval is needed in each destination country, which comprises a short dossier and a fee payable to the regulatory authority of each country. At EU level and for products that have pan-European licensing through the EMEA centralised procedure, a pan-European parallel importation license can be obtained, subject to satisfaction of the regulator of safety and a fee payable.

Where centrally authorised medicinal products are concerned, the only changes that parallel distributors may introduce to the packaging of a medicinal product are those which are strictly necessary to market the product in the destination member state (e.g. use of different language version(s) of labelling and package leaflet; or change in the package size provided the proposed size falls within the scope of the EU MA). This is slightly different from the parallel importation of medicines authorised nationally because of differences between the marketing authorisation granted by the member state of origin and the one granted by the member state of destination.

The regulatory process is rigorous and this minimises the risk of counterfeit drugs. In the UK and over a period of eight years, only one such case was recorded. However, several violations regarding repackaging, relabelling, trademarks, and inaccurate patient inserts have been reported by manufacturers to the relevant regulatory authorities. A significant number of these has been recorded in the UK. Of these, inaccuracies in patient inserts are probably the most important in terms of public health hazards, as they may provide out-of-date or even misleading information to patients and providers. Some violations have led to product recalls in some destination countries.

Parallel distributors are only allowed to procure products from a holder of a wholesale distribution authorisation in the source member state. The supplier is obliged to inform the parallel distributor of any recall activity originating with the supplier or earlier in the distribution chain including the original manufacturer that might involve products supplied to the parallel distributor. Such notifications must be handled within the parallel distributor's GMP system to confirm whether the affected product was actually received, trace its utilisation and initiate recall procedures as necessary, including contacting the local competent regulatory authority.

It is up to the trademark owner to check that the presentation after repackaging (should this occur) will not damage the reputation of the trademark owner. Problems have occurred in the past with the application of a sticker on top of the original trademark.

Parallel distributors are compliant with the national and EMEA procedures, although there have been cases where manufacturers have complained of improper handling of their products by parallel distributors.

### ***C. Institutional issues***

The way the distribution chain operates in the UK offers significant incentives to pharmacies to search for PI medicines and this process can also yield financial benefits to the NHS through the clawback.

The evidence suggests that, at least in principle, the clawback is a powerful mechanism that acts as an incentive for pharmacists to search for better deals when purchasing medicines from different sources. Parallel distributors (PDs) can usually offer significant discounts over and above locally-sourced products and, in this case, the use of PI medicines is de-facto promoted. In order to retain market share, locally-sourced products may need to be sold at the same discount off the list price, in a so-called price equalisation deal. Of course, for all this to continue to happen, sufficient quantities of PI medicines need to be available in order to guarantee the sustainability of the market and, understandably, this may not always be the case.

The clawback applies to all pharmacies, although chain pharmacies are excluded from the surveys that determine its extent. Theoretically, the objective of policy-makers is to extract the entire discount from pharmacies through the clawback, but this is not always happening, because discounts can be not only product-specific, but also pharmacy-specific. Elementary economic theory would suggest, for instance, that chain pharmacies may benefit more than single community pharmacies, simply because they have a larger purchasing power and, therefore, may be able to get better deals (discounts) from wholesalers or PDs. Out of all this, the NHS claws back a fixed (average) 10.44 per cent whereas pharmacies can retain the difference whatever this may be. It has also been suggested that discounts on generic products off the drug tariff can be even more significant. The entire process of pharmacy distribution raises questions about the economic efficiency of the system and the extent to which further savings can be achieved for the NHS.

### ***D. Market structure issues***

The UK market of parallel distributors is made up of 14 key companies who are members of, and organise, the British Association of European Pharmaceutical Distributors (BAEPD). The BAEPD is a non-profit organisation, promoting, protecting and developing the interests of its members who possess the appropriate licences granted by the Department of Health through the Medicines and Healthcare Products Regulatory Agency (MHRA) for parallel distributing. In the UK, the amount of parallel-sourced pharmaceuticals has grown significantly and steadily from 1998-2002 in money terms and in market share, which has more than doubled since 1998 to 20 per cent, whereas the share of domestically-sourced pharmaceuticals has dropped by ten per cent.

The licence holders source prescription pharmaceuticals from any member state within the European Union (EU) where it is profitable to import from and distribute their products into the supply chain in the United Kingdom, either through retail pharmacies, dispensing general practitioners or hospitals and clinics. Pharmacies have an indirect incentive to procure more from parallel importers—the average clawback currently stands at 10.44 per cent. If pharmacies achieve a higher discount on this, then they can keep the difference.

### ***E. Economic impact***

The principle of the free movement of goods within the European Union is key for the completion of the internal market and parallel trade is, in theory, a means of evening price differences across member states. In pharmaceuticals, regulation at member state level prohibits the principle of arbitrage from working efficiently, and drug prices are not necessarily responsive to the pressures of parallel trade but only to the regulatory interventions that create them at member state level.

Statutory health insurance organisations in exporting (source) countries realise no benefits, whereas, from a conceptual perspective, their counterpart organisations in destination countries may benefit in three ways: first, in the case of price differentials in the list prices of

locally-sourced and PI pharmaceuticals the price difference accrues partly or in its entirety to them. In the Netherlands and Norway, the government involves pharmacists as direct agents to maximise its financial benefits, by surrendering part of these to pharmacists. In Norway, any likely financial benefits are equally split between the government and pharmacists, whereas in the Netherlands the pharmacist, until recently, retained one third of the price difference, surrendering the remainder to the government.

The second source of potential revenue to health insurance organisations is the ‘clawback’, which, according to the evidence presented, may arise either because of invisible discounts from wholesalers and parallel traders to pharmacists (UK, the Netherlands), or as a source of compulsion to pharmacists, operating in an environment of fixed wholesale and retail margins, to procure from cheaper sources (Germany). Either way, health insurance organisations want to ensure that part of the pecuniary benefits accruing to pharmacists from more competitive purchasing are in the form of lower reimbursement to them.

The third way through which health insurance might benefit is price competition, leading to (downward) price convergence in destination countries, although one cannot ascertain the extent to which this is occurring, and it is likely to be product-specific.

Pharmacists can also benefit in countries where pharmacy margins are not determined by regulation, and the UK is a prime example of this. In this case, benefits arise from individual negotiation, whereby pharmacists can negotiate discounts with parallel importers, making it profitable to stock and dispense a parallel-imported medicine that carries the same reimbursement price as a locally-sourced one.

The benefits to patients in destination countries theoretically accrue from the lower prices of PI drugs on the assumption that patients pay a significant proportion of their medication out-of-pocket. Reducing their overall medication costs therefore improves access to essential medicines. In practice, however, European health systems, particularly in the UK, the Netherlands, Germany, Denmark and Sweden (and, perhaps, less so in Norway), provide comprehensive cover with low cost-sharing requirements. Where PI medicines have a price advantage over locally-sourced ones, the difference accrues to statutory health insurance, therefore patients continue to be unaware of such price advantages.

The empirical evidence relevant to the UK finds significant benefits to parallel distributors, modest to moderate benefits to the NHS, mostly through the clawback, and no impact on patient access to care due to lower-priced medicines. The benefits to the NHS combined with those of parallel distributors are the sum of the loss to producer surplus. There is little or no evidence on price competition from parallel trade within the UK, and little evidence on price convergence between the UK and likely exporting countries.

## Introduction

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Parallel trade, a form of arbitrage, arises either to arbitrage away international price discrimination, or to free-ride on investment made by intellectual property right (IPR) holders.<sup>1</sup> The issue of pharmaceutical parallel imports (PI) continues to generate controversy among stakeholders and has become an issue of intense debate in the global trading system.<sup>2</sup>

Pharmaceutical parallel trade has grown consistently in the European Union due to the principles of free movement of goods and the regional exhaustion of intellectual property rights (IPR), as well as a series of European Court of Justice (ECJ) rulings over the past two decades.<sup>3</sup> Parallel trade is also encouraged by the governments of several member states. This is especially so in countries where overall price levels for in-patent pharmaceuticals are at or above the European average (UK, Sweden, Denmark, Germany, the Netherlands).

Advocates of strong international patent rights (and, therefore, opponents of parallel trade) for new medicines support a global policy of banning PI, arguing that if such trade were widely allowed it would reduce profits in the research-intensive pharmaceutical sector and ultimately slow down innovation. Some advocate a global ban on parallel trade as a natural extension of IPR owners to vertically control the product chain. Their rationale for this argument lies in their conviction that there are ambiguous long-term benefits from parallel trade (PT).<sup>4</sup>

Advocates of pharmaceutical parallel trade, such as public-health authorities, maintain that it is important to be able to purchase drugs from the cheapest possible source, thus favouring an open regime for PI. Whether or not such imports actually take place, the threat that they might do, it is argued, could force manufacturers to lower prices. It is evident that policymakers both in developing countries, but also elsewhere, would place a higher weight on affordability of medicines than on promoting R&D abroad.<sup>5</sup> It has also been argued<sup>6</sup> that PIs are (weakly) attractive to a country irrespective of its tariff regime and the extent to which it is also setting a tariff or not.

Further arguments are provided on the benefits and drawbacks from allowing parallel trade among countries.<sup>7</sup> Having accounted for the differences between countries in terms of health systems (reflected in the level of patient co-payments), and in terms of drug needs (reflected in the patients' valuation for the drug), parallel trade leads to price convergence between countries, makes the individuals of the importing country better off, while making those of the exporting country worse off and decreasing the profit of the monopoly producer. In the short run, PT may yield benefits to consumers in high price markets but may harm consumers in markets that would have low prices if PT were not permitted; thus, prices across borders would not be uniform.<sup>8</sup> Furthermore, price uniformity in the presence of increasing returns to scale can have an adverse effect on all countries (both high-price and low-price).<sup>9</sup>

The European Union is very active in preventing restrictions on internal parallel imports. The first major competition policy enforcement in the EU concerned an attempted dealership territoriality within the EU; theoretical work suggests that, 'generally, policies worldwide firmly support parallel imports'.<sup>10</sup> Other than theoretical interest in the dynamics of parallel trade,<sup>11</sup> national governments and European institutions have displayed an increased level of preoccupation with the subject over the past few years, which can be attributed to a number of reasons:

- i) The differences in the methods of pricing and reimbursing pharmaceuticals across the European Union member states (see Table 1.1) result in significant price differences for the same product and product formulation among the different member states, thus enabling parallel trade (arbitrage) across borders (Table 1.2). Some prices can vary up to threefold

between high price countries and the lowest priced country, or, indeed, the average of the three lowest priced countries. This provides a very strong incentive for parallel trade to occur between the latter and the former when the opportunity arises, namely, when stocks exist and where transaction costs can be minimised.

- ii) Parallel trade has reached a significant proportion of total national pharmaceutical expenditure in many countries. Parallel imports reached nearly 20 per cent of the total UK market, 14 per cent of the Dutch market, ten per cent of the Danish and Swedish markets, and seven per cent of the German market in 2002.
- iii) Parallel trade represents an interesting—albeit difficult-to-balance—policy dilemma, touching upon the principles of free trade policy within an economic and monetary union, the determination of health and pharmaceutical policy (both of which take place at national level, and for which EU-wide competence is non-existent), and the existence or not of industrial policy in the pharmaceutical sector, whether at national or supra-national level.<sup>12</sup>

Overall, the situation in the EU follows a conflicting pattern whereby member states wish to exercise their legal right and autonomy to determine their own pharmaceutical policy; wholesalers or parallel traders perform arbitrage of pharmaceuticals across countries exercising their legal right provided by the principle of the free movement of goods; and some governments have an active industrial policy in place, with the objective of promoting innovative research and development (R&D) in the pharmaceutical sector through minimal interventions on the pricing of medicinal products.

Consequently, the paper focuses on five themes, namely legislative developments, regulatory framework, institutional policies, market structure, and economic impact. These issues are pursued in turn. We used secondary data sources and combined these with interviews with industry and regulators on the basis of a questionnaire sent to them. We did not have the opportunity to conduct interviews with parallel distributors, although the same questionnaire was addressed to them too.

Section 2 discusses the legislative framework as it has evolved over 25 years of case law at EU and national levels. Section 3 outlines the regulatory framework, its perception by regulators, and its implementation; it also discusses some of the shortcomings that have surfaced in the past eight years. Section 4 discusses the institutional framework and national policies on parallel trade as they apply in the UK. Section 5 analyses the structure of the parallel distribution market in the UK, using as benchmarks published accounts by PD companies. Section 6 reviews the literature of the economic impact of parallel trade in the UK and beyond. Section 7 draws the main conclusions.

**Table 1.1**  
**Pricing and reimbursement methodologies in selected EU countries and Norway, 2004**

Country		Main pricing/reimbursement rules relating to price setting
Denmark	a) b) c)	Pricing agreement establishing pharmacy buy-in prices until June 2002 Reimbursement according to Average European Price (AEP) rule comprising 11 EU countries plus Norway, Liechtenstein and Iceland Cost efficacy studies a requirement for price premium
France	a) b) c)	Free pricing for products that do not seek reimbursement status 2003-2006: price notification for highly innovative products (ASMR = 1 or 2) For other products: price fixing through negotiation with CEPS on the basis of various criteria (including the product's medical value, prices of comparable medicines, volume sales, conditions used, industrial presence in the country, cost-effectiveness criteria (implicit)). If the reimbursement status is granted, the product will be sold on the market only at the reimbursed price
Germany	a) b)	Price freedom for new products Reference price for off-patent sector (products subjected to generic competition; reference price for identical molecule only)
		Table 1.1 cont'd over

Country		Main pricing/reimbursement rules relating to price setting
Greece	a) b) a) b) c) d)	Price fixing for imported medicines (lowest EU price for the same molecule) Cannot grant a price unless product is marketed in one European country Requirement to be included in reimbursement lists of three of the following countries: France, Germany, Switzerland, UK, US, Sweden Clustering (reference price) for calculating the average daily treatment cost Cost-effectiveness may be requested Lowest European price rule declared unlawful by the country's constitutional court in December 2001
Italy	a) b) c) d)	AEP (all EU countries) for 'old' products and products registered with the national procedure; AEP is calculated on ex-manufacturer's price (excluding VAT), of top five selling equivalents, including generics Price negotiation (contractual model) for new and innovative products for drugs registered with the EU procedures (EMA and mutual) or for those for which AEP cannot be calculated Price freedom for non-reimbursable drugs New negotiation guidelines issued in February 2001 require: submission of cost effectiveness study, pricing and reimbursement status in other countries, commitments on volume sales and discounts to hospitals, payback clauses or price reductions or delisting if sales rise above agreed levels, data on R&D and manufacturing investment in Italy
The Netherlands	a) b) c)	Maximum price fixing [AEP] (twice per year) through European price comparisons (reference countries are Germany, France, Belgium, UK) AEP system giving equal weight to all alternative products (since 2000) Use of pharmacoeconomic studies for reimbursement of products requesting price premium
Portugal	a) b) c) d)	Two-step process with MoFinance agreeing to the maximum price for every new product and, subsequently INFARMED processes reimbursement applications Price control (average pricing of Spain, France and Italy); some room for price negotiation Submission of 'cost-benefit' data to support reimbursement status Payback system is currently in operation until the end of 2003, whereby industry pays back 64.5% of any excess on agreed upon target growth rates
Spain	a) b) c) d) e)	Price control through negotiation on a cost-plus basis, taking into account expected sales and allowing specific margins for profits (12-18% of allowable cost), advertising (12-16% of allowable costs), and R&D conducted in Spain International price comparisons for active ingredient when difficulties arise in assessing the transfer price of a molecule Price-volume agreement for expensive products Pact stability agreement with government also promoting R&D Payback clause intensified
Sweden	a) b) c) d) e) f) g) h) i)	Price control if reimbursement is sought; otherwise free pricing Reimbursement price takes into account price in 10 European countries; exchange rates used for conversion Price should be lower than Denmark, the Netherlands, Germany, Switzerland and similar to those in Norway and Finland Annual negotiations between the industry and the National Social Insurance Board for price revisions Price-volume agreements for innovative products No price increases are allowed for two years after launch of products reimbursed by RFV Products seeking price increases of more than 10% after their first two years need to obtain RFV approval Health economic evaluation if price premium is requested Price volume agreement for innovative products
UK	a) b) c) d)	PPRS: agreement with industry on profit control, renewed on 13 July 1999, for a five-year period Price cut, as part of PPRS, of 4.5% Free price modulation from 1 January 2001 but keeping the 4.5% price cut range overall Guidance on cost-effectiveness by NICE becomes binding
Norway	a) b) c) d)	Free pricing unless requesting reimbursement European (EU and EEA) price comparisons, with R&D costs and prices of competitor products being taken into account New product price setting by means of taking the average of the two lowest prices of Sweden, Denmark, Finland, UK, Ireland, France, Germany, the Netherlands, Belgium, and Austria Prices of new and expensive products need to be ratified by Parliament

Source: Kanavos, P., 2004.

**Table 1.2**  
**PP prices for 19 products adjusted by DDD and pack size**

Original	Norway	Belgium	Germany	Sweden	Denmark	UK	Nether-lands	Spain	Portugal	Italy	Greece	France	Ireland	Austria
Atorvastatin	0.78	0.86	1.37	1.04	0.72	1.01	0.95	0.96	0.91	0.63	0.55	0.91	0.89	0.97
Pravastatin	1.25	1.08	1.63	1.00	0.98	1.67	1.04	1.58	1.11	0.91	0.66	1.07	1.55	0.92
Simvastatin	1.43	1.28	1.06	N/A	0.81	1.25	1.12	1.19	0.82	0.74	0.62	0.80	1.13	0.96
Captopril	0.48	0.62	0.28	0.21	0.46	0.58	0.54	0.26	0.56	0.30	0.38	0.61	0.50	0.77
Enalapril	0.25	0.29	0.20	N/A	0.22	0.59	0.30	0.19	0.28	0.28	0.19	0.46	0.41	0.24
Quinapril	N/A	0.76	0.45	0.49	0.37	0.38	0.88	0.19	0.36	0.37	0.27	0.53	0.75	0.43
Ramipril	0.32	0.51	0.48	0.31	0.17	0.60	0.69	0.21	0.28	0.24	0.18	0.40	0.35	0.36
Losartan	0.83	0.93	0.80	0.85	0.63	0.97	0.87	0.63	0.77	0.69	0.58	0.92	0.77	0.47
Valsartan	0.82	0.59	0.80	0.82	0.60	0.88	0.86	0.45	0.72	0.62	0.39	0.87	0.75	0.77
Clozapine	0.20	0.27	0.25	0.18	0.19	0.92	0.28	0.13	0.28	0.29	0.11	0.30	N/A	0.10
Olanzapine	4.80	5.60	5.78	5.37	3.81	5.48	5.19	3.57	3.90	3.60	3.30	4.83	6.07	5.28
Risperidone	3.98	4.23	5.54	4.08	2.68	5.21	5.47	2.87	3.22	2.93	2.25	3.65	5.03	5.23
Lansoprazole	1.37	2.01	1.84	1.15	0.85	1.33	1.93	1.07	0.90	1.53	1.05	1.68	1.66	1.57
Omeprazole	1.89	2.24	1.77	1.83	N/A	1.60	2.09	0.43	1.66	1.50	0.84	1.86	1.77	1.57
Pantoprazole	1.33	2.01	2.32	1.16	0.83	1.33	1.88	1.27	1.34	1.28	1.10	1.65	1.40	1.57
Citalopram	1.02	1.08	1.12	0.66	0.75	0.90	1.18	0.73	N/A	0.75	0.68	0.90	0.97	0.97
Fluoxetine	0.97	1.04	1.16	0.85	0.78	1.51	1.38	0.53	0.69	0.56	0.65	0.93	0.90	0.61
Paroxetine	N/A	1.31	1.16	0.90	0.91	0.93	1.11	0.80	0.86	0.77	0.69	0.90	0.90	0.56
Sertraline	1.08	1.22	1.11	1.12	0.82	0.85	1.31	0.72	0.76	0.87	0.55	0.84	1.36	0.88

Source: Kanavos, P., Costa Font, J., Merkur, S. and Gemmil, M., 'The Economic Impact of Parallel Trade in European Member States', LSE Health and Social Care, London School of Economics; January 2004.

## Legislative Background

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### ***2.1 Parallel Trade and the EU Treaties***

In order to establish a single market for pharmaceuticals in the European Union (EU) the European Commission (EC) endeavours to preserve the free movement of goods between member states through competition in the pharmaceutical market.<sup>1</sup> Article 28 of the Treaty prohibits all measures which have the equivalent quantitative effect of restricting the free movement of goods between member states, including national intellectual or industrial property rights. Exceptions to this rule fall under Article 30 and justify the protection of industrial and commercial property rights ('specific subject matter' only), the exhaustion of rights and the pursuit of public health. Furthermore, Article 295 stipulates that the Treaty shall in no way prejudice the rules in member states governing the system of property ownership.

The doctrine of exhaustion of intellectual property rights has reconsidered the balance between Article 28 and Articles 30 and 295. The European Court of Justice (ECJ) holds the view that once a product has been legitimately put on the market in one member state, it is a breach of Article 28 to prevent the product from being resold in another member state, even if the product is protected by the exclusivity granted by a patent or other intellectual property right in the latter state.

In the EU, exhaustion of intellectual property rights is by first sale. Once the product has been sold in one member state by or with the consent of the holder of an intellectual property right in another, the latter cannot exercise that right to restrain commercial import of the protected product. However, Article 30 allows a trademark holder to exercise his rights to block the sale of an imported product bearing his trademark, if its original packaging has been modified in a way beyond what is necessary to permit its sale in the importing member state. These bans or restrictions may not in any way constitute either means of arbitrary discriminations or hidden restrictions to trade between member states. On the other hand, member states can prohibit or restrict imports and exports for reasons of protecting public health and human life. Despite this, if the health and life of humans can be as effectively protected by measures which do not restrict intra-Community trade, practices that restrict trade are not compatible with the Treaty.<sup>2</sup>

The starting point of the case law governing parallel trade began outside the realm of pharmaceutical products. The landmark case of *Cassis de Dijon*<sup>3</sup> confirmed for the first time that Article 28 covers measures applying in the same way to domestic and imported goods ('indistinctly applicable measures'). In the absence of harmonised Community rules, the member states retain the power to lay down rules governing the composition, manufacture, packaging, and presentation of products. Then again, they are required to admit to their country products lawfully produced and marketed in other member states. The *Cassis de Dijon* case showed that the importation of foodstuffs lawfully produced and marketed in other member states may only be restricted in the absence of harmonisation by such rules where they are: a) necessary in order to satisfy mandatory requirements such as the effectiveness of fiscal supervision, the protection of public health, the fairness of commercial transactions and the protection of consumers; b) *proportionate* to the desired objective, namely that national measures must not be more restrictive than reasonably required; and c) the means of achieving that objective which least hinders trade. The three requirements of necessity, proportionality and means which least hinders trade are to be regarded as expressions of the general principle of 'proportionality'.

Competition between economic players is protected under Articles 81 and 82 of the EC Treaty. Any agreements preventing, restricting or distorting competition, or affecting trade, are prohibited. This includes limiting or controlling markets, imposing export bans<sup>4</sup> and engaging in differential treatment with trading parties thereby placing them at a competitive disadvantage.

Under Article 82, any abuse by a party in a dominant position within the common market is prohibited. This would include vertically integrated supply chains where a manufacturer may abuse their position over a distributor. Examples of this abuse include the exploitation of dual pricing<sup>5</sup> and pricing systems not allowing for a rational profit margin for economic players thus creating an unfavourable market. Greece has been accused of such practices because its pharmaceutical pricing system routinely takes the lowest European price as the Greek price. Nevertheless, 'unilateral' abusive action by a non-dominant firm affecting trade has created challenges and relaxed this law in a recent ruling on the case of Bayer-Adalat by the ECJ.<sup>6</sup>

Parallel trade is therefore based on the fundamental principles of the free movement of goods and the exhaustion of intellectual property rights. The endeavour to assure a single intra-EU market is further reflected in numerous decisions by the ECJ. These judgments are transformed into national law by the member states and interpreted by rulings of national courts as well as executions through the relevant national authorities. Together they define the legal framework for parallel trade of medicinal products in the EU member states.<sup>7</sup>

## ***2.2. Issues arising from the ECJ jurisprudence***

Tables 2.1 and 2.2 summarise the main issues in parallel trade, the relevant cases and the respective outcomes. To ensure the creation of a single market, emphasis has been placed on the principle of the free movement of goods, provided that a) the product has been marketed in the exporting State; and b) that it has been marketed by or with the permission of the patent holder.

The ECJ has highlighted that the principle of relaxation of controls by national authorities in member states is closely related to the principle of co-operation of authorities of member states. Member states are obliged to treat imported products under the present market authorisation for a pharmaceutical product if it already exists provided the product is therapeutically identical, i.e. contains the same active ingredient, in the same amount, and is available in the same dosage form. The burden of proof rests on the public authority within the member state to challenge the parallel imported product if they believe the product displays scientific uncertainty, different therapeutic effects of the many variants of the same medicine, or uses of different excipients.<sup>8</sup>

Charging different prices for domestic and foreign use of the same product (dual pricing) is an issue that remains to be sorted but is in principle prohibited when the practice attempts to inhibit parallel trade in the single market. Case law also forbids importing member states from using measures from the exporting country, including price regulation, to inhibit the free movement of goods.

In addition, agreements between manufacturers and wholesalers with the objective of the dominant party (manufacturers) to prevent, restrict or distort competition within the single market, or for a national market, are forbidden. When companies impose bans on exports by written actions, continuous behaviour and bilateral agreements between entities, they are infringing on EU law. Limiting supplies to wholesalers is also a form of infringement; however, as detailed in the latest Bayer-Adalat verdict, these restrictions were relaxed. If actions are shown to be unilateral (no agreement between undertakings), with no outright ban on exports and no monitoring of the final destination of the product, such implicit exporting restrictions do not infringe on EU law.

New regulations in Spain and Greece, imposed through the distribution of circulars, require companies to report the quantities of products they export. Although this reporting is deemed to be confidential, the establishment of databases may lead to detailed information on the final destination of products. The response of EU institutions to these national interventions is unknown and unclear at this stage, but it is certain that the parties affected will bring them to their attention.

The legal status of any industrial or intellectual property right must be protected without damaging the principle of free movement. Thus, the concept of the specific subject matter can be applied to determine this in some cases. Only under legitimate reasons can a pharmaceutical company restrict parallel trade by objecting to the re-marketing of their own products. If parallel traders desire to repackage a medicine, they must adhere to the principles of proportionality and

satisfy specific criteria including the protection of the condition of the product and the reputation of the trademark, giving the trademark owner notice and stating it has been repackaged. Reboxing (as opposed to over-labelling) is deemed objectively necessary if, without such packaging, effective access to the market would be impeded as a result of strong resistance from a significant proportion of consumers to the relabelled product. Advanced notice of approximately 15 working days must be given to the trademark holder of the intended repackaging. Additionally, at their request, the parallel trader must supply a sample of the product before it goes on sale.

To date there are considerable restrictions as to the options for parallel distributors when repackaging branded products. Pharmaceutical companies can reject specific changes such as the use of the parallel importer's house style for the get-up of the packs, removal of the trademark owner's mark or name from the front of the pack, prominent use of the parallel importer's name on the front of packs or use of capital letters for their name on the side of boxes, and placement of the parallel importer's name prominently on blister packs for drugs inside the boxing. These results may to a large degree render re-boxing commercially unattractive. Despite this, the use of simple colour schemes does not violate the above guidance. Even with all the detailed guidance on repackaging, parallel importers are not required to repackage products, thus creating less work for them. A further implication on importers is that they must maintain the specific size and form of the presentation when considering the central market authorisation of a medicinal product. These specific conventions are intended to prevent consumers from being misled and to protect public health.

### **2.3. Conclusion**

As a result of numerous cases heard before the European Court of Justice (ECJ) since the late 1960s, a number of issues appear to have been resolved; in this context, specific policy implications of parallel trade include that:

- a) Parallel distributors do not have to repackage products, but may do so if they adhere to specific guidance, such as the protection of the condition of the product and the reputation of the trademark, giving the trademark owner notice and stating on the product that it has been repackaged;
- b) Member states are required to afford simplified national registration rules for parallel importers such that if the health authorities of the destination country already possess the relevant information for the identical medicine, no further obligation is placed on the parallel importer;
- c) Provided the medicines are therapeutically identical, i.e. contain the same active ingredient in the same amount and same dosage form, there is no obligation for a parallel imported product to have a common origin to a domestic brand;
- d) Member states can disallow parallel imports for reasons of protecting public health and safety, including differences in product formulation and package size modifications that may mislead consumers (Article 30 of the EU Treaty);
- e) Manufacturers can manage their inventory so long as there is no outright ban on exports, no monitoring of the final destination of the product, and no agreement between undertakings (manufacturers & wholesalers);
- f) Important issues remain unresolved but are likely to be heard before the ECJ in the near future; most notably, these include (i) dual pricing, in the context of defining the geographical boundaries of a (national) market and (ii) the abuse of dominant position and the criteria for defining it. Two pending cases, one on dual pricing (Spain) and one on abuse of dominant position (Greece), which will be heard by the ECJ in 2005 are likely to influence future policy direction on parallel trade, depending on the court's rulings;
- g) With ten new member states having joined the EU on 1 May 2004, it will also be necessary to observe how these will affect the future of parallel trade and how the EU will apply its governing principles, especially the principle of derogation.

**Table 2.1**  
**European pharmaceutical parallel trade and relevant European Court of Justice (ECJ) cases**

Case Name and Year
Cases 56 and 58/64 Consten and Grundig v. Commission (1966)
Case 15/74 Centrafarm BV v. Sterling Drug Inc. (1974)
Case 104/75 Adrian DePeijper, Managing Director of Centrafarm BV (1976)
Case 102/77 Hoffmann-La Roche & Co. AG v. Centrafarm (1978)
Case 3/78 Centrafarm BV v. American Home Products (1978)
Case 120/78 Cassis de Dijon (1979)
Case 187/80 Merck & Co. Inc. v. Stephar BV and Petrus Stephanus Exler (1982)
Case 227/82 Leendert van Bennekom (1983)
Case 174/82 Officier van Justitie v. Sandoz BV (1983)
Case 19/84, Pharmon BV v. Hoechst AC (1985)
Cases 87 and 88/85 Société coopérative des laboratoires de pharmacie Legia and Louis Gyselinx et fils - Cophalux v. Minister of Health (1986)
Case C-277/87 Sandoz Prodotti Farmaceutici SpA v. Commission of the European Communities (1990)
Case C-201/94 Regina v. The Medicines Control Agency, ex parte Smith & Nephew Pharmaceuticals Ltd and Primecrown Ltd v. The Medicine Control Agency (1996)
Cases C-267/95 and C-268/95 Merck & Co Inc and others v. Primecrown Ltd and others and Beecham Group plc v. Europharm of Worthing Ltd (1997)
Cases C-427/93 and C-429/93, C-436/93 Bristol-Myers Squibb v. Paranova (1997)
Case C-355/96 and Case C-355/96 Silhouette International v. Hartlauer Handelgesellschaft [1998] E.T.M.R. 539. International v. Hartlauer Handelgesellschaft (1998)
Case C-414/99 Zino Davidoff SA v. A&G Imports Ltd (1999)
Case C-94/98 The Queen, ex parte Rhone-Poulenc Rorer Ltd and May & Baker Ltd v. The Licensing Authority established by the Medicines Act 1968 (1999)
Case C-379/97 Pharmacia & Upjohn v. Paranova (1999)
Case T-41/96 Bayer AG v. Commission of the European Communities (2000)
Cases: IV/36.957/F3 Glaxo Wellcome, IV/36.997/F3 Aseprofar and Fedifar, IV/37.121/F3 Spain Pharma, IV/37.138/F3 BAI, IV/37.380/F3 EAEP (2001) Regina v. Secretary of State for Health ex parte (1) British Association of European Pharmaceutical Distributors (formerly Association of Pharmaceutical Importers) (2) Dowelhurst Limited, and Others (2002)
Case C-433/00 Aventis Pharma Deutschland GmbH v. Kohlpharma GmbH and MTK Pharma Vertriebs-GmbH (2002)
Cases C-443/99 and 143/00 Merck, Sharp & Dohme GmbH v. Paranova Pharmazeutika Handels GmbH and Boehringer Ingelheim GmbH, Glaxo Group Ltd and others v. Dowelhurst Ltd and Swingward Ltd. (2002)
Case C-112/02 Kohlpharma GmbH v. Federal Republic of Germany (2003)
Cases C-2/01P and C-3/01P Bundesverband der Arzneimittel-Importeure and Commission of the European Communities v. Bayer AG (2004)

Source: Merkur, S.M. and Kanavos, P., 'EU parallel trade of pharmaceutical products: What does the law allow?' Mimeo, LSE Health and Social Care, April 2004.

**Table 2.2**  
**Parallel trade in the EU: Main issues, relevant cases and outcomes**

Issues	Relevant Cases	EU Law and Jurisprudence
<ul style="list-style-type: none"> <li>➤ Exhaustion of rights</li> <li>➤ Free movement of goods</li> </ul>	<ul style="list-style-type: none"> <li>• Merck v. Stephar</li> <li>• Pharmon v. Hoechst</li> <li>• Merck v. Primecrown</li> <li>• Silhouette</li> </ul>	Once an original manufacturer puts a product on the market in a member state, they have exercised their right and the rules of free movement apply. The inability to obtain full patent protection does not affect this exhaustion of rights; however, this only applies within the EEA.
<ul style="list-style-type: none"> <li>➤ Differences in the product</li> <li>➤ Relaxation of controls</li> <li>➤ Co-operation of authorities</li> </ul>	<ul style="list-style-type: none"> <li>• De Peijper</li> <li>• Smith and Nephew</li> <li>• Société coopérative and Louis Gyselinx</li> <li>• Kohlpharma v. the Federal Republic of Germany</li> <li>• Leendert van Bennekom</li> <li>• Rhône-Poulenc Rorer</li> </ul>	Medicines must be therapeutically identical for parallel trade between countries, i.e. same active ingredient, same amount, same dosage form, and bioequivalent. A member state is only permitted to require a new market authorisation for a pharmaceutical product that is already covered by a market authorisation in another EU member state for specific reasons. These include: a) the existence of scientific uncertainty about the constituents; b) different therapeutic effects of the many variants of the same medicine; and c) the use of different excipients.
<ul style="list-style-type: none"> <li>➤ Patent protection</li> <li>➤ Dual Pricing</li> <li>➤ Price regulation</li> </ul>	<ul style="list-style-type: none"> <li>• Centrafarm v. Sterling</li> <li>• Glaxo Wellcome</li> <li>• Merck v. Primecrown</li> <li>• Judicial review of the 1999 PPRS</li> </ul>	The patentee has the exclusive right to manufacture and put into circulation industrial or commercial products for the first time and oppose infringements related to the 'specific subject matter' of the patent right. The manufacturer may not engage in dual pricing in an attempt to prevent exportation. Furthermore, price regulation from the exporting state is prohibited from restricting the free movement of goods.
<ul style="list-style-type: none"> <li>➤ Banning export</li> <li>➤ Limiting supplies</li> </ul>	<ul style="list-style-type: none"> <li>• Consten and Grundig v. the Commission</li> <li>• Sandoz v. the Commission</li> <li>• Bayer AG v. the Commission</li> </ul>	The patentee can prohibit exports implicitly so long as: a) there is no agreement between undertakings; b) the ban is unwritten; and c) there is no systematic monitoring of the final destination of the product.
<ul style="list-style-type: none"> <li>➤ Repackaging</li> <li>➤ Modifying package size</li> </ul>	<ul style="list-style-type: none"> <li>• Hoffmann-La Roche v. Centrafarm</li> <li>• Pharmacia &amp; Upjohn v. Paranova</li> <li>• Bristol-Myers Squibb v. Paranova</li> <li>• Merck, Sharp &amp; Dohme v. Paranova</li> <li>• Boehringer Ingelheim and Others v. Swingward Ltd</li> <li>• Aventis Pharma Deutschland v. Kohlpharma and MTK Pharma</li> </ul>	In repackaging, the importer must: a) not affect the original condition of the product, including the inclusion of instructions and information; b) state on the packaging that it has been repackaged; c) not damage the reputation of the trademark through the presentation; d) give advanced notice to the trademark holder—the ECJ suggested 15 working days; e) only perform 'necessary' repackaging, i.e. the least intrusive method and not solely for the purpose of gaining commercial advantage; and f) not modify the package size under the specific market authorisation.

Source: Merkur, S.M. and Kanavos, P., 'EU parallel trade of pharmaceutical products: What does the law allow?' Mimeo, LSE Health and Social Care, April 2004.

## Regulatory Issues

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Within the EU, products are approved either through the centralised procedure (submission to the European Medicines Evaluation Agency—EMA), or through the mutual recognition (decentralised) procedure. The mutual recognition procedure involves submitting to a national regulatory agency and, following approval for marketing authorisation from this national agency, all other agencies throughout the EU automatically recognise this marketing authorisation (MA). The same processes apply for parallel distribution (PD) of a product approved through the centralised or the decentralised procedures.

For both the centralised and the decentralised procedures, the regulatory authorities apply the *acquis communautaire*, i.e. the legislative framework as it has been developed through EU law and the ECJ jurisprudence on the subject. The context for *centrally* authorised products is different from the parallel importation of medicines authorised *nationally* because of differences, which can exist between the marketing authorisation granted by the member state of origin and the one granted by the member state of destination.

Parallel distributors will source products from wholesalers in lower price countries. Before they sell the imported products in any market they must obtain marketing authorisation for these products. Once they have obtained the necessary parallel licenses, distributors will either sell directly to pharmacies, or may utilise wholesalers' distribution networks and allow the latter to distribute directly to pharmacies. It is estimated that parallel distributors may also re-export a share of imported products but a majority is sold within the primary destination country. The same may hold for wholesalers once they have obtained products from parallel distributors. After wholesalers and pharmacies have purchased products from parallel distributors, they will then be dispensed to patients and the NHS will subsequently reimburse the cost of medicines dispensed to pharmacies, subject to a clawback. Graph 3.1 illustrates this in a flow diagram at the end of this section.

The following section outlines the requirements for PD under the centralised and decentralised procedures in theory and in practice, as well as discussing some of the relevant regulatory shortcomings, with particular emphasis on the UK. Material for this section has been collected from the European Medicines Evaluation Agency (EMA) and, through a questionnaire and interviews, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and the pharmaceutical industry.

### **3.1 Parallel distribution notification (centralised procedure)**

#### *Distribution issues within the EU*

For distributing a centrally approved product within the EU, parallel distributors need first to notify the EU Marketing Authorisation Holder (MAH) and not the national affiliate of the company in question. The only changes that parallel distributors may introduce to the packaging of a centrally authorised medicinal product are those which are strictly necessary to market the product in the destination member state (e.g. different language version[s] of labelling and package leaflet; change in the packet size provided the proposed size falls within the scope of the EU MA).

#### *Regulatory requirements*

In addition to a cover letter outlining the case, the PD must submit the following documents:

- i) The 'Notification of parallel distribution of a centrally authorised medicinal product' form, signed and dated by the official contact person

ii) Information relating to the proposed PD notification, in particular:

- Details of the PD
- Details of the medicinal product (i.e. invented name, strength, pharmaceutical form) and authorisation number in the Community register of medicinal products (i.e. EU number)
- Details of the MAH
- The member state(s) of destination
- Certification that the condition of the product has not been affected
- Confirmation that the applicable fee of €3,480 has been paid (see Table 3.1)

The PD also needs to attach to the application form:

- a) Mock-ups of the new outer and inner packaging of the medicinal product as proposed by the PD
- b) Mock-ups of the package leaflet of the medicinal product as proposed by the PD (two copies, in colour), or, if available, two colour copies of the repackaged specimen (including outer, inner packaging and package leaflet)
- c) A full copy of the PD's wholesale distribution licence
- d) Or a full copy of the Manufacturing Authorisation or both if the re-packager is different from the PD

The PD is only allowed to distribute presentations that are covered by the Community Marketing Authorisation for that particular centrally authorised medicinal product. A separate notification should be submitted for each presentation of a given medicinal product.

#### *Application review process*

Once the PD notification has been received, the EMEA will check its validity within five working days and inform the parallel distributor of the start of the regulatory check for any missing/incorrect information. The EMEA will check the conformity of the proposed labelling and package leaflet within 30 days after validation of the notification and will notify the parallel distributor of any objections/comments. If there are no objections, or when any objections have been completely addressed by the parallel distributor, the EMEA issues a notice and sends it to the parallel distributor, the national authority of the member state of destination and the MAH of the medicinal product, informing them that the regulatory check has been completed and that parallel distribution can commence.

The EMEA no longer routinely requests the submission of a specimen prior to issuing the Notice. A colour copy of the repackaged sales presentation will be requested by the EMEA within the initial notification and, if this is not acceptable, the EMEA may still request the submission of a specimen.

#### *Multiple licenses*

Since an EU marketing authorisation is specific for a given centrally authorised product to be marketed under that particular invented name **it is not acceptable** for the PD to interchange them in the context of parallel distribution.

Parallel distributors wishing to distribute products which are available on the EU market under two or more invented names need to submit to the EMEA a separate PD notification for each centrally authorised product. The name given to a medicinal product may be either a) an invented name; or b) a common/scientific name together with the name of the manufacturer.

#### *Bundle-packs*

The EMEA does not accept any proposals from parallel distributors to bundle existing presentations of a centrally authorised product to create a larger pack-size, even if this pack-size

is covered by the Community marketing authorisation of the concerned medicinal product. This is because different presentations are subject to separate central marketing authorisations.

#### *Manufacturing and wholesale distribution licenses*

The European Court of Justice (ECJ), in order to explain what will always require a valid manufacturing authorisation, has defined repackaging as:

- a) 'removal of blister packs from the original external packaging and their insertion into new external packaging' and
- b) 'addition to the packaging of new user instructions or information or the fixing of self-stick labels'

The parallel distributor can repackage products themselves or they may be outsourced to another company, subject in either case to the holding of a valid manufacturing authorisation. A PD is normally engaged in activities defined as wholesale distribution and will need to hold a wholesale distribution authorisation.

#### *(Re)packaging and (re)labelling*

The parallel distributor must mention the manufacturer of the MAH on the medicinal product, according to EU law and complemented by ECJ case law. Although the ECJ case law requires the repackager and the MAH manufacturer to be identified on the medicinal product, the EMEA also recommends the mentioning of the 'parallel distributor' as follows:

##### *Outer labelling*

On the outer labelling the following text should be added in the language for the member state of destination:

'Parallel distributed and repackaged by ... (name and address)'

'Parallel distributed by ... and repackaged by ...' (in case PD and repackager are different)

Parallel distributors are allowed to identify more than one repackager in the initial PD notification provided they include two sets of mock-ups, each clearly identifying one of the repackagers. Where the PD has notified more than one repackager in this notification, he should ensure to only mention on the outer label the repackager for the concerned batch.

##### *Inner labelling*

If practical, the name of the PD and repackager should preferably be included on the inner labelling as well, but it is not compulsory.

It is acceptable to mention only the name:

'Parallel distributed and repackaged by ... (name)'

'Parallel distributed by ... and repackaged by ...' (in case PD and repackager are different)

Where the PD has notified more than one repackager in this notification, he should ensure to only mention on the inner label the repackager for the concerned batch.

The particulars shall appear in the official language or languages of the member state where the product is placed on the market. This does not prevent these particulars being indicated in several languages, provided that the particulars appear in all the languages used.

The addition of a PD internal code to packaging material is considered by the EMEA as good practice and therefore acceptable, provided it is not being presented as part of the core text of the labelling and package leaflet. The original batch number must always be retained. This includes the mentioning of a 're-pack batch' or the addition of a prefix or suffix to the original batch number to reflect additional repackaging activities.

#### *Notifications of a change*

PD must ensure that the proposed labelling and package leaflet remain in conformity with the annexes to the latest Commission Decision granting or amending the market authorisation.

The PD should submit a 'Notification of a change' form, stating the scope of change if amendments have been made to the annexes of the Community marketing authorisation for a centrally authorised medicinal product, or when the parallel distributor wants to change information submitted in the initial PD notification.

The EMEA performs a detailed check of the proposed labelling and package leaflet in the initial notification but leaves the implementation of any further updates to the PD. PD are still requested to inform the EMEA on the date of implementation of the changes and the EMEA will establish a 'spot-check' system instead of performing a detailed check of the updated labelling and/or package leaflet.

PD notifications of change should be accompanied with a cover letter and should include:

- i) The 'notification of a change for PD of a centrally authorised medicinal product' form signed and dated by the official contact person;
- ii) Details of the MAH;
- iii) Scope of the change;
- iv) Signature on the form;
- v) Mock-ups of the outer and inner packaging of the medicinal product;
- vi) Mock-ups of the package leaflet clearly mentioning the date of the Commission Decision texts used;
- vii) Two colour copies of the repackaged specimen, if available.

### *PD Inspections*

The EMEA cannot request an inspection of a PD. The EMEA inspections will check the validity of the wholesale, distribution and manufacturing licenses submitted as part of a PD notification. The responsibility for any actions remains with the competent authorities (drug regulatory authorities) of the respective member states.

### *Registered trademark issues*

In accordance with ECJ case law it is up to the trademark owner to check if the presentation after repackaging is not such as to damage the reputation of the trademark owner.

### *Handling product defects or recalls*

If a defect occurs with a PD product when the product leaves the manufacturer or develops during subsequent handling, the PD has responsibilities:

- a) Manufacturers are required to have a system for recording and reviewing complaints and effective recall. The competent authority will assist the PD in the recall process and will initiate the rapid alert system accordingly. A PD should ensure that the marketing authorisation holder is informed of any recall initiated by the PD;
- b) Suppliers are obliged to inform the PD of any recall activity originating with the supplier or earlier in the distribution chain. Notifications must be handled within the PD GMP system to confirm whether the affected product was actually received, trace its utilisation and initiate recall procedures, including contacting the local competent authority.

## **3.2 Parallel distribution notification (decentralised procedure)**

### *(i) The regulatory framework*

National agencies have developed their own regulations, which stem from EU law and ECJ jurisprudence, to ensure that PD medicines meet the same safety and quality criteria as their equivalent locally-sourced ones. National authorities also have the right to apply the relevant fees for a parallel distribution notification (Table 3.1), which in all cases are significantly lower than fees applicable to all new drug applications (NDA).

Under the EEC treaty on the free movement of goods, the UK is required to permit the importation of medicinal products from other member states providing that certain conditions are met. The imported product may not be marketed until the licensing authority has granted a licence; this is an offence for which a fine can be imposed on summary conviction.

All the following conditions must be met before an application can be considered under the parallel import procedures. The imported product must:

- a) be a product which is to be imported from a member state of the European Economic Area (EEA);
- b) be a proprietary medicinal product (as defined in Article 1 of EC Directive 2001/83/EC) for human use;
- c) be covered by a currently valid marketing authorisation granted in accordance with EC Directive 2001/83/EC by the regulatory authority of a member state of the EEA;
- d) have no differences, having therapeutic effect, from a product covered by a UK marketing authorisation;
- e) have a common origin, i.e. be made by, or under licence to, the same company, or a member of the same group of companies, as the holder of the marketing authorisation for the UK product; or be made under licence to a company (inside or outside the EEA) which has also licensed the manufacture of the UK product.

The labelling and patient information leaflet of the product must also meet the requirements set out in directive 2001/83/EC and must be in English. Labelling requirements may be met by either repackaging the product or affixing labels to the original external packaging. The original batch number of the product must appear on the carton if the product is re-boxed.

The parallel importer may apply for any product name he or she chooses. This is normally the UK brand name, the brand name in the exporting country or the generic name. Brand names are not acceptable, however, if they can be confused with the name of a different product already on the UK market.

A PD licence is granted for five years and will continue if both the UK licence and the EU marketing authorisation to which it relates remain in force. If either marketing authorisation is revoked on grounds relating to safety, the UK PD will be withdrawn. If the EU marketing authorisation is withdrawn, it may be possible to continue to market the product in the UK, but only if the UK PD satisfies the strict criteria that the European Court of Justice have set for the survival of PDs in these circumstances.

#### (ii) *The application of the regulatory framework in practice*

In order to validate the process described above, we contacted Mr Geoffrey Lay, Pharmaceutical enquiries, Parallel Imports, Homoeopathics, Drug/Device Unit, of the UK MHRA and provided him with a questionnaire seeking to acquire information on regulatory procedures, dealing with safety issues, labelling and counterfeiting, among others. A copy of the questionnaire is attached in Appendix 1 (p. 81).

In this questionnaire, we first of all sought MHRA's perception of the regulatory procedures regarding the approval of parallel imported medicines and how these procedures compare with locally-sourced products. According to MHRA, there is no specific law regarding the approval of parallel imported medicines, but there are *communications of law* from the EU and these may sometimes be compromised by rulings of the ECJ. Therefore, the situation seems to be one of 'making the law up as one goes along'. Generally, if the conditions are met, a license is granted. But it is felt that there is so much case law surrounding parallel imported drugs that it has muddied the waters and it is now very difficult to turn licenses down. It is MHRA's perception that parallel distributors rarely supply adequate information and it is often the case that the authorities have to return to the original manufacturers for the correct information. In the vast majority of cases, this is no problem. If there are complications though, drugs can get held up in the system for a long time.

Second, we enquired about how MHRA addresses issues of safety, inadequate labelling and counterfeiting. With regards to safety, products should be made to the same standards, and if patients do suffer reactions to PD drugs, they can send in a yellow (complaint) card and the MHRA will follow up the complaint in the usual way. The MHRA will look at the active substances and this is not an issue to do with a PD drug. With regards to inadequate labelling, PD's have to give samples of labelling as part of licensing requirements. It was felt that labelling had been getting better until GSK took PD's to court over trademark issues. Lay's personal feeling regarding labelling was that, ultimately, the manufacturers over-influence the system. Regarding counterfeiting—an issue that is frequently raised by the manufacturers—in reality, there has been only one case so far of a parallel-distributed product and that was raised by a PD. This instance resulted in a court case and a fine. Our respondent, Geoffrey Lay, has been with MHRA for eight years and does not see counterfeiting as a major issue, with only 1-2 cases occurring over this period that he can remember.<sup>1</sup>

Third, we asked about the extent to which there had been any experience with expired drugs, labelling and packaging problems, or unsafe handling. Regarding expired drugs, there is no available data or information, but the feeling is that, in general, because pharmacists have quick turnovers it is very difficult to see problems arising in this regard. In terms of labelling and packaging, there have been several problems in the past; the majority of problems have occurred as a result of incorrect translations. Labelling of PD products is an 'extra step' in the usual process of bringing drugs to market and therefore it is naturally liable to problems. There are 1-2 labelling recalls a year and the most common complaint is about labels describing the days or weeks when the product should be taken by the patient. However, there is no requirement to put such labels on packs. Finally, with regard to unsafe handling, since 2003 more products have had to be re-configured. Medicine inspectors have reported that batch sizes from manufacturers have been getting smaller. This has caused more problems, as there are now more opportunities for the PD to mix products up as the PDs create new batch sizes.

Fourth, we wanted to be informed of the technology that exists to minimise the (potential) effects of counterfeit and/or expired drugs, labelling problems or unsafe handling. The response was that, currently, there is no such technology available—and expiry dates are not something PDs can get around. The MHRA's 'police' do any necessary checking and they follow up any complaints.

Our final question enquired about the extent to which there were unapproved drugs crossing the border. The response was that there are systems in place to allow doctors to use medicines not marketed in the UK. An example of this would be for patients who are allergic to existing treatments or who are at a stage in their disease when they have tried all other alternatives. Overall, parallel distributors are not interested in importing unapproved drugs.

### ***3.3 Regulatory shortcomings***

Despite the seemingly clear regulatory framework, a number of problems have arisen from the parallel distribution of medicines throughout the EU in general, and the UK in particular, since the latter has one of the most dynamic parallel distribution markets. The nature of these problems is threefold:

- i) There are product shortages in source countries for products that are aggressively traded between countries;
- ii) Regulatory violations in relation to (re) packaging, (re) labelling, and patient inserts are affecting the quality of the offered product;
- iii) Uncertainty concerning the implementation of the derogation principle by the member states in the cases of parallel importation for the newly acceding Eastern European countries.

Each of the above aspects is briefly examined in turn by focusing on the UK, where appropriate.

*i) Reported product shortages*

There is always a fear that arbitrage may affect negatively the availability of products in the exporting country, if higher returns are available for it elsewhere. Over the past three years, there have been several isolated cases and one more generalised case to the extent that several pharmaceutical companies have complained to their respective trade associations that parallel trade has led to individual product shortages. These complaints have arisen in Greece, Italy, Spain, the Netherlands and France.

The extent of parallel exportation has forced a reaction by the Spanish regulatory authorities so that, as of May 2003, a law was adopted according to which wholesalers are required to reveal the destination of the products sold to them by the manufacturers.

On other occasions (e.g. in Denmark, a country with long history of parallel importation), parallel distributors have not adequately foreseen local demand in destination countries, have run out of a product and consequently raised their prices above the prices of the company holding the MA for the said product. In Denmark, where pharmacies must always dispense the cheapest product on the shelf unless the doctor bans substitution, this has led to situations where the drug manufacturer has unexpectedly had to supply the product for the entire market.

*ii) Regulatory violations*

It is important to stress that no cases of actual product modification (e.g. tampering with product formulation) have been reported. This would be a violation of the manufacturer's IP rights, would be beyond the scope of parallel trade and would lead to the amended product being regarded as a counterfeit.

Several cases have been reported over the past three years of regulatory violations pertaining to problems with repackaging, relabelling and the quality or the contents of the patient insert. This has led to formal complaints by the manufacturers and, sometimes, to litigation. Problems with repackaging and relabelling may not be life-threatening but the issue remains that they may: (i) influence patients' perception of or regard for the product; (ii) confuse patients who may be used to one type of packaging, but suddenly have to accept a different pack for the same product, often in a language they do not understand; and (iii) damage product reputation. Problems with patient inserts can be more serious and could potentially lead to threats to public health, if the information is not accurately presented or if it is out-of-date.

The majority of problems with repackaging, relabelling and patient inserts have occurred in a handful of destination countries: the Netherlands, the UK, Germany, Sweden and Denmark. Whereas repackaging and relabelling per se are seldom threats to public health, they can lead to product recall by the manufacturers if they feel that the product presentation is altered significantly and beyond what is necessary.

The most common problems concerning labelling and packaging were related to:

- a) Incorrect stickers included in the pack;
- b) Formulation and composition differences between source and destination country, which are disallowed;
- c) Providing misleading information to practitioners about how to administer a certain treatment;
- d) Wrong information provided on the pack about the coordinates of the MA holder
- e) Failure to translate the days of the week on the calendar side of the blister and problematic over-stickering;
- f) Removal of tablets from different packs to put them together in a larger pack, or, on the contrary, just cut and over-stuck blisters to obtain a pack with a smaller number of pills according to the characteristics of the products sold in the destination country;
- g) The name of the manufacturer not being mentioned on the new packaging and labels being stuck on the pack in a way they mask the items required by European legislation (e.g. batch number).

On several occasions, problematic packaging and labelling has been the primary reason for product recalls, particularly in Germany, where parallel imports have been growing rapidly since 2000. Indeed, there were over 50 recalls for parallel-imported products between January 2002 and August 2003.

The most common problems concerning patient inserts were related to:

- a) Wrong information on the amount of the tablets included in the pack;
- b) Wrong country of origin for the pack in question;
- c) Old address of the originator company appearing on self-made leaflets by parallel distributors;
- d) Misleading information on the use of products and how to keep them. Problems with the product's expiry date;
- e) Complaints that patient leaflets in parallel imported products were just summaries or simply not readable;
- f) Complaints that the language used in the packages and blisters was different from the one in the destination country and, therefore, unreadable for several patients;
- g) No translation of the leaflet into the destination country language;
- h) Omissions from and errors in the patient leaflet; and an absence of updated information on patient leaflet.

Finally, trademark problems have not been uncommon among parallel-distributed products. Parallel distributors have been known to put a sticker on the trademark with the generic name of the product, replace the trademark used in the source country by the one used in the destination country and completely cover the original trademark without acknowledging the manufacturer's name on the pack.

### iii) *EU accession and the derogation principle*

On 1 May 2004, the EU admitted ten new member states, eight from former Eastern Europe (Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Slovakia and Slovenia), plus Cyprus and Malta. Parallel trade from the newly admitted member states will be guided by the application of the principle of derogation. The principle of derogation applies to the eight Eastern European new members, but does not apply to Cyprus and Malta. It means that where intellectual property rights for individual products are not the same in the eight accession countries as compared with the EU-15, then no parallel trade is allowed from any of the eight Eastern European member states to EU-15. However, parallel trade within the territory comprising the ten new member states is allowed. The EU-15 have signed up to a document outlining the new rules and accepting the principle of derogation, but there are few signs concerning the potential for enforcing this. This may pose a threat of exportation from one of the eight newly acceding Eastern European countries to the old EU-15, including the UK, if sufficient price differences exist, without due consideration for trademark rights.

### **3.4. Concluding remarks on regulatory issues**

There are few hurdles before gaining marketing authorisation of parallel-imported pharmaceuticals through the centralised and the national regulatory procedures. Testing is not needed, the product name can remain the same (although national regulatory authorities typically advise for the brand name prevailing in the member state of importation to be used), and the costs of the application are substantially lower than those of a new substance or a generic product. One key barrier to parallel importing of pharmaceuticals is the need for relabelling of the product and the insertion of a patient leaflet in the language of the destination member state. In some member states (e.g. the Netherlands), pharmacists can set up a wholesaling company and maximise their purchasing economies. The costs of obtaining a license for doing this does not appear to be a barrier.

There are regulatory controls for parallel-imported pharmaceuticals in each destination country. Regulatory approval is needed in each destination country, which comprises a short

dossier and a fee payable to the regulatory authority of each country. At EU level and for products that have pan-European licensing through the EMEA centralised procedure, a pan-European parallel importation license can be obtained, subject to satisfaction of the regulator of safety and a fee payable.

Where centrally authorised medicinal products are concerned, the only changes that parallel distributors may introduce to the packaging of a medicinal product are those which are strictly necessary to market the product in the destination member state (e.g. use of different language version[s] of labelling and package leaflet; or change in the package size provided the proposed size falls within the scope of the EU MA). This is slightly different from the parallel importation of medicines authorised nationally because of differences between the marketing authorisation granted by the member state of origin and the one granted by the member state of destination.

The regulatory process is rigorous and this minimises the risk of counterfeit drugs. In the UK and over a period of eight years, only one such case was recorded. However, several violations regarding repackaging, relabelling, trademarks, and inaccurate patient inserts have been reported by manufacturers to the relevant regulatory authorities. A significant number of these has been recorded in the UK. Of these, inaccuracies in patient inserts are probably the most important in terms of public health hazards, as they may provide out-of-date or even misleading information to patients and providers. Some violations have led to product recalls in some destination countries.

Parallel distributors are only allowed to procure products from a holder of a wholesale distribution authorisation in the source member state. The supplier is obliged to inform the parallel distributor of any recall activity originating with the supplier or earlier in the distribution chain including the original manufacturer that might involve products supplied to the parallel distributor. Such notifications must be handled within the parallel distributor's GMP system to confirm whether the affected product was actually received, trace its utilisation and initiate recall procedures as necessary, including contacting the local competent regulatory authority.

It is up to the trademark owner to check if the presentation after repackaging (should this occur) will not damage the reputation of the trademark owner. Problems have occurred in the past with the application of a sticker on top of the original trademark.

Parallel distributors are compliant with the national and EMEA procedures, although there have been cases where manufacturers have complained of improper handling of their products by parallel distributors.

**Table 3.1**  
***Duration of marketing authorisation and direct costs of regulatory approval in selected European countries, 2004***

Country	Duration of marketing authorisation	Cost of obtaining marketing authorisation
Denmark	5 years	Annual fee of DKK7,950 (€1,071) plus application fee of DKK15,095 (€2,033.4) or renewal fee of DKK13,975 (€1,882.5)
France	5 years; application needs to be filed 3 months before expiry to extend authorisation	N/A
Germany	5 years; application needs to be filed 3 months before expiry to extend authorisation	€1,380
Greece	5 years	€180
Italy	5 years	€524.20 per product
The Netherlands	Valid as long as branded equivalent has marketing authorisation	€1,465 per product €5,672.25 per year for holding a PI license
Portugal	N/A	N/A
Spain	5 years	N/A
Sweden	5 years	SEK15,000 (€1,637)
UK	5 years (but normally continues in force only so long as both UK licence and EEA marketing authorisation remain in force)	£1,465 (€2,125)
Norway	5 years given that original has been marketed in EEA for 6 years	NOK70,000 - 80,000 (€8,489 - €9,701.8) plus control fee of 0.7% of the turnover of the MA holder
EMEA (for centrally approved products)	5 years	€3,480 for each parallel distribution notification

Source: Author's own research from direct contacts with national regulatory authorities and the EMEA, 2004.

**Graph 3.1**

***Flow chart illustrating the flow of parallel-traded pharmaceutical products***

## Institutional Policies Encouraging the use of PI Medicines

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Evidence from national sources suggests that parallel trade in pharmaceuticals has intensified over the past six years (Table 4.1, p. 30) to 2002, especially in high-price EU countries. More recent evidence, however, suggests that parallel trade has slowed down in the key destination countries. In key markets such as Germany and the UK this may be partly due to the introduction of various pharmaceutical sector reform measures (e.g. the requirement in Germany that a PI medicine has to be ten per cent cheaper than the locally-sourced one), or indeed to limitations in product in EU member states. Over the same period, other member states, for which data is available, have experienced significant increases in exports. There are issues concerning interests that national stakeholders (in particular, health insurance organisations, patients and pharmacies) have from the conduct of pharmaceutical parallel trade and whether or not national governments have initiated policies that allow them to benefit. In this light, the discussion in this section focuses around:

- 4.1 Institutional policies directly encouraging the dispensing of parallel-imported pharmaceuticals by pharmacies and financial benefits to institutional players (both health insurance organisations and pharmacies) through parallel distribution;
- 4.2 Other national policies indirectly influencing PI activities at national level;
- 4.3 Patient access to medicines.

From a conceptual standpoint, the theory of arbitrage argues that the availability of parallel-distributed products can potentially result in lower prices for domestic equivalents than would otherwise be the case. Essentially, arbitrage results in three effects that may impact on health insurance organisations' ability to benefit financially from its conduct:

- a) Price differences between locally-sourced and PI pharmaceuticals. In this case, it is assumed that PI product(s) will be priced lower than the equivalent locally-sourced product(s) in order to attract market share;
- b) The likelihood of price competition between what appears to be perfect substitutes.<sup>1</sup> Health insurance organisations should benefit over the long term from better price deals in both locally-sourced and PI pharmaceuticals. From an economic standpoint, this would also imply a rather competitive PI market structure with parallel distributors engaging in competition among themselves and undercutting each other by offering better price deals to pharmacies and health insurers. It also assumes that the original manufacturer is engaging in price competition over the medium to long term;
- c) The impact of discounts (whether price discounts or volume deals) offered to pharmacists in countries where margins are fixed by law. Discounts may in principle be operating at the margin of legality, but are impossible to account for, and are therefore invisible. Such discounts can be approximated where relevant information exists, e.g. in the UK and the Netherlands, but even in these cases their precise level (i.e. on a product-by-product basis) is impossible to gauge. Nevertheless, discounts, whether formal or informal, result in direct benefits to pharmacies with no additional benefit to statutory health insurance organisations unless there is a clawback system in place. There are no benefits to patients unless the latter contribute all or a significant part of the cost of medicines out-of-pocket.

Within this broad framework, the variety of products that are imported is quite significant. In the UK, parallel imported products have one or more of the following characteristics:

- i) Price differentials between locally-sourced and PI can be significant, depending on the source country (see also Table 1.2); it seems as though the price difference is one of the most

important variables affecting the availability of PI products. However, it is not always possible to import from the cheapest possible source due to product not being available in sufficient quantities. In this case, and in order to guarantee product availability through this channel, an alternative source may be found;

- ii) Source countries have traditionally included Spain, France, Italy, Greece and Portugal, without the possibility of other EU member states exporting smaller quantities if and when the opportunity arises;
- iii) The most common presentations for locally-sourced pharmaceuticals are also available as PI, although this also seems to be influenced somewhat by the extent of the product market.

#### ***4.1 UK institutional policies encouraging the dispensing of parallel-imported pharmaceuticals***

Institutional policies refer to measures explicitly taken by statutory health insurance organisations to lower the cost of reimbursed pharmaceuticals. These policies may specifically target PI pharmaceuticals or may refer to the entire market, including PI. Typically, high-price countries, such as Denmark, Germany, the Netherlands, Norway, Sweden and the United Kingdom, have set up such policies either encouraging directly the dispensing of PI products, or allowing their healthcare systems to benefit from their use, or both.

In the UK, the way through which use of PI is encouraged is associated with the way the distribution chain operates, whereas the key mechanism allowing the NHS to benefit is the 'clawback'. Pharmacy remuneration differs in the UK from other EU countries, in that it is not subjected to fixed (progressive or regressive) margins, other than a dispensing fee per prescription. This allows UK pharmacies, whether independent or chain, to procure from sources that can provide them with the highest discount off drug list prices. Every pharmacy in the UK, whether it uses parallel-distributed products or not, is subject to the Department of Health's clawback. The 'clawback' system (discount recovery scale) directly encourages pharmacists to procure more cost-effectively. The DoH takes into consideration the 'Discount to Pharmacy' given by the wholesaler or parallel distributor to the pharmacist. Chain pharmacies are excluded from the inquiry. The DoH reimburses pharmacists based on the NHS list price minus the 'clawback' which currently ranges between 6.51 per cent and 13.2 per cent depending on the number of prescriptions dispensed each month. Most pharmacies are falling into the 10.44 per cent bracket. In the latter case, for every £100 of claims submitted by a pharmacy to the NHS for reimbursement, the NHS pays back £89.56.

The exceptions to this case are the 'zero discount scheme' products in the drug tariff. This scheme applies to products that have a high cost for wholesalers in terms of storage and distribution. It affects about 500 products including 300 fridge-lines (e.g. vaccines), expensive items such as betaferon and controlled drugs that require extensive record keeping. For these products the wholesalers do not discount the product to the pharmacist and the DoH reimburses the pharmacist at NHS-price level without deducting the clawback.

Considering the flat fee structure of the clawback relative to the number of prescriptions, pharmacies have an indirect incentive to procure more from parallel importers, or, indeed, obtain the so-called price-equalisation deals from official wholesalers, enabling them to keep a significant proportion of the overall discount given. If pharmacies achieve a higher discount than the clawback then they can keep the difference. Other than discounts given to pharmacies, PI pharmaceuticals do not have an incentive to be priced lower than the list price.

Evidence from the Pharmaceutical Services Negotiating Committee (PSNC) illustrates that savings from PI would be on average 17.43 per cent, whereas actual discounts of the top ten products to individual pharmacies range from 1.6 per cent to 24.3 per cent compared with the NHS list price.<sup>2</sup> Profits are maximised by dispensing more PI drugs, whilst keeping the returns to the DoH unchanged through the fixed clawback scales. This may have an upward knock-on effect on future clawback scales but this would have prospective rather than retrospective action. The DoH estimates 2001-2002 place savings from this activity at £100 million (€143 million),<sup>3</sup> whereas other estimates elevate the impact of the clawback from parallel imports to the sum of £134 million (€192 million) for 2002.<sup>4</sup>

#### **4.2 Policies indirectly encouraging (or discouraging) PI**

In the UK, the current PPRS Agreement (1999—2004) has allowed free price modulation with effect from 1 January 2001, which has been interpreted by many, including the UK parallel distributors' association, as a policy that would allow UK-based pharmaceutical companies to fluctuate prices of drugs that are vulnerable to parallel importation in order to restrict their import potential. This presumption has led to a judicial review of the PPRS, which found in favour of the UK government. This was because of a lack of robust evidence that free price modulation would encourage pharmaceutical manufacturers to lower prices enough in order to discourage parallel importation.

#### **4.3 The impact of PI on patient access to medicines**

An argument for parallel trade is that it reduces the cost of medicines to the end-users, i.e. patients, thereby improving access. In order to assess this argument one would need to distinguish between medicines that are reimbursed and those that are not reimbursed. For non-reimbursed medicines, patients would benefit directly from lower drug costs if pharmacies pass on the entire or part of the price difference between parallel-imported and locally-sourced medicines to the consumer. The extent to which this is happening is unknown, but taking into account the incentive structure for pharmacists, it is doubtful that this is happening, as there is no compulsion by health insurance for the latter to do so.

In the case of medicines that are reimbursed by health insurance, patients may benefit from pharmaceutical parallel trade through two channels, direct and indirect. The direct channel relates to the reduced cost of medicines to them and the impact this may have on patient out-of-pocket expenditure. The argument is that as patients pay a significant fraction or all the cost of their medicines out-of-pocket, then parallel trade, through lower prices, can reduce this cost to the patient and enhance patient access to needed medicines. A condition for this to occur is that health insurance allows any price differential between parallel imported and locally-sourced medicines to be shifted to patients rather than directly accruing to the health insurer and/or pharmacy. The analysis in the previous sections suggests that this may not be the case and health insurance would appropriate all or a significant proportion of any price differences. Even if this was not the case, however, patients would realise pecuniary benefits, but this would depend on the structure of cost sharing in individual countries. In the UK patients do not realise the cost of medicines because they pay fixed fee per prescription. In countries that do have co-insurance and/or an annual deductible it is possible to realise benefits, unless the beneficiary is exempt. Overall, the size of these benefits is likely to be marginal.

The indirect channel relates to savings that health insurance organisations such as the NHS make through parallel imports. In this case, patients may benefit from the re-allocation of such benefits to purchase better care for patients.

#### **4.4 Policy lessons and conclusions**

The way the distribution chain operates in the UK offers significant incentives to pharmacies to search for PI medicines and this process can also yield financial benefits to the NHS through the clawback.

The evidence suggests that, at least in principle, the clawback is a powerful mechanism that acts as an incentive for pharmacists to search for better deals when purchasing medicines from different sources. PDs can usually offer significant discounts over and above locally-sourced products and, in this case, the use of PI medicines is de facto promoted. In order to retain market share, locally-sourced products may need to be sold at the same discount off the list price, in a so-called price equalisation deal. Of course, for all this to continue to happen, sufficient quantities of PI medicines need to be available in order to guarantee the sustainability of the market and, understandably, this may not always be the case.

The clawback applies to all pharmacies, although chain pharmacies are excluded from the surveys that determine its extent. Theoretically, the objective of policy-makers is to extract the

entire discount from pharmacies through the clawback, but this is not always happening, because discounts can be not only product-specific, but also pharmacy-specific. Elementary economic theory would suggest, for instance, that chain pharmacies may benefit more than single community pharmacies, simply because they have a larger purchasing power and, therefore, may be able to get better deals (discounts) from wholesalers or PDs. Out of all this, the NHS claws back a fixed (average) 10.44 per cent whereas pharmacies can retain the difference whatever this may be. It has also been suggested that discounts on generic products off the drug tariff can be even more significant. The entire process of pharmacy distribution raises questions about the economic efficiency of the system and the extent to which further savings can be achieved for the NHS.

**Table 4.1**  
**Market value of pharmaceutical parallel imports and their share as a percentage of the total pharmaceutical market in selected EU countries<sup>1</sup>**

	1997	1998	1999	2000	2001	2002
UK (£ m) <sup>5</sup>	na na	462 9.5%	633 11.9%	749 13.6%	1,076 17.1%	1,346 19.8%
Sweden (SEK m)	270 1.9%	1,012 6.2%	1,402 7.7%	1,732 8.6%	2,011 9.3%	2,309 10.1%
Denmark (DKK m)	554.6 9.1%	656.2 10%	700.3 10%	781.4 10.2%	835.5 9.9%	917.2 9.7%
Germany (€ m)	216.7 1.7%	256.6 1.9%	331.1 2.3%	504 3.2%	800.3 4.7%	1,296.3 7.01%
Greece <sup>2</sup> (€ m)	14.0 0.9%	107.0 7.7%	173.7 10.7%	308.1 16.5%	514.3 24.4%	556.7 <sup>3</sup> 21.6% <sup>4</sup>
Netherlands (€ m)	357 14%	363 14%	374 14.5%	365 13.5%	424 14.3%	456 14%

Notes:

- 1 Data and information are not available for a number of countries as follows: (a) in France, there are currently no parallel imports and the regulatory framework is currently being set up; data for parallel exports were not available either; (b) in Italy, there is no data available because regulation for parallel imports is very general and loose. As of June 2003, there were four registrations for parallel imports; data on parallel exports were not available either; (c) in Portugal, there are no official data for parallel imports or parallel exports; (d) in Spain, there are no official data for parallel imports or exports; currently, there are two parallel imported pharmaceuticals, one from France and one from Greece.
- 2 Data for Greece are pharmaceutical parallel exports.
- 3 Estimates.
- 4 Expressed as a share of the retail market in each year.
- 5 Official UK data (from the Prescription Pricing Authority) does not identify parallel imported products.

Sources: Sweden: IHE, 2003; Denmark: LFN, 2003; Germany: AOK, 2003; Greece: IKA/IOBE, 2003; the Netherlands: SFK, 2003; UK: IMS, 2003.

## UK Market Structure

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The parallel trade in pharmaceuticals dates back to the 1970s when a number of pharmacists realised that drug prices varied significantly between member states of the EEC. To take advantage of this they established small wholesale businesses from their dispensaries, supplying other local pharmacies initially and, subsequently, the wider UK health service. In 2002, the UK market for parallel-distributed pharmaceuticals represented £1,300 million (€2,000 million) and is the largest market in the EU.

The UK market of parallel distributors is made up of 14 key companies who are members of, and organise, the British Association of European Pharmaceutical Distributors (BAEPD). The BAEPD is a non-profit organisation, promoting, protecting and developing the interests of its members who possess the appropriate licences granted by the Department of Health through MHRA for parallel distributing.<sup>1</sup>

The licence holders source prescription pharmaceuticals from any member state within the European Union (EU) and distribute their products into the supply chain in the United Kingdom, through either retail pharmacies, dispensing general practitioners or hospitals and clinics.

Table 5.1 (p. 33) illustrates the sizes of 13 of the key parallel distributors in the UK, in terms of turnover, profits and fixed assets. These figures are sourced from the relevant companies' accounts in the years shown. Turnover figures range from £9.9 million p.a. in 2003 (G Pharma Ltd) to £270 million p.a. (Waymade Healthcare Plc). The five-firm concentration ratio was 65.4 per cent in 2001/2002 and 64 per cent in 2002/2003. An interesting element from this table is the fact that Jumbogate's operating profit fell sharply between 2002 and 2003 from £7.9m to negative £5.4m. This can be explained by a sharp rise in administrative expenses, and specifically wages and salaries, which increased from £330,964 in 2002 to £15,350,875 in 2003. However, the number of employees remained constant at 12. Directors' remuneration and other emoluments increased from £72,000 in 2002 to £6,072,000 in 2003.

There is considerable diversity between the sizes of the parallel distributors' turnover, ranging from £9.9m to £270m (Tables 5.1 and 5.2). Waymade is clearly the largest parallel distributor in terms of turnover, operating profit and gross profit, making twice as much gross profit as its nearest rival, Necessity Supplies Ltd, with £33.9m compared to £16.3m. However, even though Waymade is the company with the largest operating profit (£16.8m), Necessity Supplies manages to return £14.7m as operating profit on much less turnover.

In comparison to 2002 figures, in 2003 Necessity Supplies Ltd suffered a fall in turnover by £25m. This fall was mainly attributed to the UK market, where turnover dropped by nearly £22m. Turnover in the EU market fell by £2.5m and the market in the rest of the world fell by £0.9m.<sup>2</sup> However, for the parallel distributors in general, turnovers increased by between £10-20m and the trend has been for a growing industry. There were a few exceptions (Doncaster Pharmaceuticals, G Pharma) but these were marginal decreases in turnover compared to Necessity Supplies. 2003 figures for Waymade, Intercare Distribution, Stephar Ltd and Beachcourse Ltd were unavailable at the time of writing because the company accounts were not published.

Many parallel distributors stated in their company accounts that it would not be in the interests of the company to provide data on how their turnover is divided by geographical market. Where data was obtained, Table 5.3 (p. 35) below illustrates the division of turnover by geographical split. Unfortunately, only two of the parallel distributors released data on how their turnover is divided by class of business, as shown in Table 5.4 (p. 36).

Despite the lack of data from the company accounts of parallel distributors, a huge majority of their parallel imported drugs are sold within the UK. Between 2002 and 2003 there is a clear

trend that the amount of parallel imported drugs being sold in the UK is growing faster in proportion to those being sold in the rest of the EU (Table 5.4). This is likely to be exportation of UK-sourced drugs to other countries, rather than re-exportation.

In terms of gross profits, Waymade Healthcare Plc is the industry's largest company, with gross profits of £33.9m in 2002 (Table 5.5, p. 37). This was double the nearest rival, Necessity Supplies, and over three times as much as its other rivals. Due to its large fall in turnover, Necessity Supplies suffered a £1.8m fall in gross profits. However, where figures for 2002-03 were available, Jumbogate, Munro Wholesale Ltd and Lexon Ltd realised increased gross profits of between £1-1.5m and the general trend for the industry in parallel with increased turnovers was similar, or increased, gross profits.

Waymade and Necessity Supplies are by far the most profitable parallel distributors, achieving twice as much profit as their nearest competitors, but Necessity Supplies' ratio of profit/turnover is far higher than that of Waymade, at 10.2 per cent compared to 6.2 per cent. The average percentage of profit on turnover of individual companies is five per cent. This seems to be consistent with the industry's acknowledgement of the amount of profit-taking, but three companies, Chemilines, Jumbogate and Necessity Supplies, are taking profits at double or more the five per cent average. If this were not the case, the average profits made on turnovers would probably be less than five per cent. (However, the ratio of profit/turnover of the 13 companies' total operating profit to the total turnover is 18.8 per cent).

Due to the nature of the industry, the parallel distributors do not own large amounts of fixed assets in relation to turnover. Nine of the thirteen parallel distributors own £1.5m worth of fixed assets or less, which will mainly include factories/warehouses and machinery. Some companies also have some fixed asset investments, such as Waymade Healthcare which has £0.6m, but on the whole there is no need for parallel distributors to own vast amounts of fixed assets (Table 5.7, p. 39).

Unlike parallel distributors, full-line wholesalers supply the whole range of pharmaceuticals, which include branded drugs, generics, and, potentially also, PI drugs. There are three national full-line wholesalers in the UK: Gehe UK (AAH), Alliance UniChem and Phoenix (a national wholesaler formed from five regional full-line wholesalers). Short-line wholesalers are generally those who concentrate on parallel imports medical supplies and generics, who have been described in detail above. Table 5.8 (p. 40) below illustrates the market share and profitability of full-line wholesalers in 1997/98.

UniChem set up OTC Direct, its own subsidiary short-line wholesaler, in September 1996 as an 'inquiry unit' to investigate why UniChem was losing first-line OTC clients. OTC Direct now specialises in buying and selling generics and parallel-imported pharmaceuticals. The link between full- and short-line wholesalers is difficult to uncover but it does exist, with many full-line wholesalers often distributing the parallel-distributed drugs of short-line wholesalers. Table 5.9 (p. 40) compares the growth in full- and short-line wholesalers between 1992-99.

Interestingly, the majority of parallel import licenses are granted to non-BAEPD members. However, membership of the BAEPD requires members to be of a certain size and it is estimated that 75 per cent of UK parallel trade is conducted by the BAEPD members. Therefore, the fact that a majority of PI licenses are granted to non-BAEPD members would indicate that these products are not products with huge market share and are likely to be niche products and not imported in great volumes (Table 5.10, p. 41).

**Table 5.1**  
**Company financial highlights of 13 members of BAEPD**

Company	Year	Turnover (£m)	Fixed Assets (£m)	Gross Profit <sup>1</sup>	Operating Profit <sup>1</sup>	Operating Profit/Turnover (%)	Operating Profit/Fixed Assets (%)
Beachcourse Ltd	2001	16.0	0.6	1.6	1.1	6.88	183.33
	2002	28.8	0.7	2.6	1.7	5.90	242.86
Chemilines Ltd	2002	47.8	0.3	6.8	5.8	12.13	1,933.33
	2003	60.3	1.5	5.9	4.4	7.30	293.33
Doncaster Pharmaceuticals Ltd	2002	32.4	0.3	2.9	0.7	2.16	233.33
	2003	30.6	0.4	2.9	0.6	1.96	150.00
Dowelhurst Ltd	2002	193.8	1.1	9.9	5.9	3.04	536.36
	2003	208.4	1.0	9.8	7.9	3.79	790.00
G Pharma Ltd	2002	9.9	0.2	0.9	0.4	4.04	200.00
	2003	8.7	n/a	0.7	0.2	2.30	n/a
Intercare Distribution Ltd <sup>2</sup>	2001	127.4	0.3	10.3	5.4	4.24	1,800.00
	2002	143.1	1.0	12.7	6.4	4.47	640.00
Interport Ltd	2002	72.0	1.5	4.4	0.7	0.97	46.67
	2003	87.7	2.2	5.7	3.7	4.21	168.18
Jumbogate Ltd	2002	83.1	0.5	8.7	7.9	9.51	1,580.00
	2003	97.1	0.4	10.3	-5.4	-5.56	-1,350.00
Lexon (UK) Ltd	2002	47.5	3.2	4.8	2.0	4.21	62.50
	2003	65.2	3.7	6.0	1.7	2.61	45.95
Munro Wholesale Ltd	2002	96.4	3.2	5.2	0.3	0.31	9.38
	2003	110.7	3.2	6.1	0.8	0.72	25.00
Necessity Supplies Ltd	2002	144.4	0.9	16.3	14.7	10.18	1,633.33
	2003	119.3	1.0	14.5	11.9	9.97	1,190.00
Stephar (UK) Ltd	2001	46.4	7.3	10.0	1.0	2.16	13.70
	2002	51.3	7.3	10.7	2.2	4.29	30.14
Waymade Healthcare Plc	2001	236.7	7.0	29.7	15.2	6.42	217.14
	2002	270.0	6.9	33.9	16.8	6.22	243.48
<b>Total</b>	<b>2002</b>	<b>1,220.5</b>	<b>27.1</b>	<b>119.8</b>	<b>65.5</b>	<b>-</b>	<b>-</b>

Notes:

- 1 Gross profit is calculated as profit after the cost of sales has been deducted; operating profit is the profit after administrative expenses have been deducted.
- 2 It is estimated that only 15 per cent of Intercare's turnover is due to parallel trade (personal communication, EAEPD).

Source: Individual company accounts sourced from Companies House, April 2004.

**Table 5.2**  
**Parallel distribution companies ranked by turnover**

Company	Turnover (2002) £m	Turnover (2003) £m	Fixed Assets £m	Gross Profit £m	Operating Profit £m	Operating Profit/Turnover (%)	Operating Profit/Fixed Assets (%)
Waymade Healthcare Plc	270.0	-	6.9	33.9	16.8 (1st)	6.22 4th	243.48 (6th)
Dowelhurst Ltd	193.8	208.4	1.1	9.9	5.9 (5th)	3.04 10th	536.36 (5th)
Necessity Supplies Ltd	144.4	119.3	0.9	16.3	14.7 (2nd)	10.18 (2nd)	1,633.33 (2nd)
Intercare Distribution Ltd	143.1	-	1.0	12.7	6.4 (4th)	4.47 (6th)	640.00 (4th)
Munro Wholesale Ltd	96.4	110.7	3.2	5.2	0.3 (13th)	0.31 (13th)	9.38 (13th)
Jumbogate Ltd	83.1	97.1	0.5	8.7	7.9 (3rd)	9.51 (3rd)	1,580.00 (3rd)
Interport Ltd	72.0	87.8	1.5	4.4	0.7 (10th=)	0.97 (12th)	46.67 (11th)
Stephar (UK) Ltd	51.3	-	7.3	10.7	2.2 (7th)	4.29 (7th)	30.14 (12th)
Chemilines Ltd	47.8	60.3	0.3	6.8	5.8 (6th)	12.13 (1st)	1,933.33 (1st)
Lexon (UK) Ltd	47.5	65.2	3.2	4.8	2.0 (8th)	4.21 (8th)	62.50 (10th)
Doncaster Pharmaceuticals	32.4	30.6	0.3	2.9	0.7 (10th=)	2.16 (11th)	233.33 (8th)
Beachcourse Ltd	28.8	-	0.7	2.6	1.7 (9th)	5.90 (5th)	242.86 (7th)
G Pharma Ltd	9.9	8.7	0.2	0.9	0.4 (12th)	4.04 (9th)	200.00 (9th)
<b>Total</b>	<b>1,220.5</b>	<b>-</b>	<b>27.1</b>	<b>119.8</b>	<b>65.5</b>	(Average = 5.18)	(Average = 568.56)

Source: Companies House, April 2004.

**Table 5.3**  
**Company turnover split by geographical market (where data was available)**

<b>Lexon (UK) Ltd</b>				
<b>Geographical Market</b>	<b>2002 (£m)</b>	<b>2002 (%)</b>	<b>2003 £m</b>	<b>2003 (%)</b>
UK	72.0	100	87.8	100
Overseas*	0.001	-	0.04	-
<b>Total</b>	<b>72.0</b>	<b>100</b>	<b>87.8</b>	<b>100</b>
<b>Jumbogate Ltd</b>				
<b>Geographical Market</b>	<b>2002 (£m)</b>	<b>2002 (%)</b>	<b>2003 (£m)</b>	<b>2003 (%)</b>
UK	82.2	98.9	94.8	97.6
EU*	0.6	0.7	2.0	2.0
Rest of world*	0.3	0.4	0.2	0.4
<b>Total</b>	<b>83.1</b>	<b>100.0</b>	<b>97.1</b>	<b>100.0</b>
<b>Lexon (UK) Ltd</b>				
<b>Geographical Market</b>	<b>2002 (£m)</b>	<b>2002 (%)</b>	<b>2003 (£m)</b>	<b>2003 (%)</b>
UK	47.5	100	64.9	99.5
Rest of the world*	0.02	-	0.3	0.5
<b>Total</b>	<b>47.5</b>	<b>100</b>	<b>65.2</b>	<b>100.0</b>
<b>Munro Wholesale</b>				
<b>Geographical Market</b>	<b>2002 (£m)</b>	<b>2002 (%)</b>	<b>2003 (£m)</b>	<b>2003 (%)</b>
UK	74.5	77.5	94.0	85
Export*	21.7	22.5	16.7	15
<b>Total</b>	<b>96.4</b>	<b>100.0</b>	<b>110.7</b>	<b>100</b>
<b>Necessity Supplies Ltd</b>				
<b>Geographical Market</b>	<b>2002 (£m)</b>	<b>2002 (%)</b>	<b>2003 (£m)</b>	<b>2003 (%)</b>
UK	137.3	95.0	115.6	96.8
EU*	6.0	4.1	3.5	3.0
Rest of world*	1.0	0.9	0.1	0.2
<b>Total</b>	<b>144.4</b>	<b>100.0</b>	<b>119.3</b>	<b>100.0</b>

\* It is not clear from the company accounts whether exports to the EU/Rest of World are first exports from the UK or re-exports. Also, there is no information in the company accounts as to where the products of the parallel distributors are sourced.

Source: Companies House, April 2004.

**Table 5.4**  
**PD company turnover split by class of business (where data was available)**

<b>Jumbogate Ltd</b>			
<b>Class of business</b>	<b>2001</b>	<b>2002 (£m)</b>	<b>2003 (£m)</b>
Wholesale	-	83.00	96.9
Retail - NHS	-	0.10	0.2
Retail - counter	-	0.02	0.04
<b>Total</b>	-	<b>83.12</b>	<b>97.15</b>
<b>Stephar (UK) Ltd</b>			
<b>Class of business</b>	<b>2001</b>	<b>2002</b>	<b>2003</b>
Wholesale	24.4	27.1	-
Retail	22.0	24.1	-
<b>Total</b>	<b>46.4</b>	<b>51.3</b>	-

Source: Companies House, April 2004.

**Table 5.5**  
**PD companies ranked by gross profit (2002)**

Company	Gross Profit (2002)	Gross Profit (2003)	Turnover (£m)	Fixed Assets (£m)	Operating Profit (£m)	Operating Profit/Turnover (%)	Operating Profit/Fixed Assets (%)
Waymade Healthcare Plc	33.9	-	270.0	6.9	16.8 (1 <sup>st</sup> )	6.22 (4th)	243.48 (6th)
Necessity Supplies Ltd	16.3	14.5	144.4	0.9	14.7 (2nd)	10.18 (2nd)	1,633.33 (2nd)
Intercare Distribution Ltd	12.7	-	143.1	1.0	6.4 (4th)	4.47 (6th)	640.00 (4th)
Stephar (UK) Ltd	10.7	-	51.3	7.3	2.2 (7th)	4.29 (7th)	30.14 (12th)
Dowelhurst Ltd	9.9	9.8	193.8	1.1	5.9 (5th)	3.04 (10th)	536.36 (5th)
Jumbogate	8.7	10.3	83.1	0.5	7.9 (3rd)	9.51 (3rd)	1,580.00 (3rd)
Munro Wholesale Ltd	5.2	6.1	96.4	3.2	0.3 (13th)	0.31 (13th)	9.38 (13th)
Chemilines	6.8	5.9	47.8	0.3	5.8 (6th)	12.13 (1st)	1,933.33 (1st)
Lexon (UK) Ltd	4.8	6.0	47.5	3.2	2.0 (8th)	4.21 (8th)	62.50 (10th)
Interport	4.4	5.7	72.0	1.5	0.7 (10 <sup>th</sup> =)	0.97 (12th)	46.67 (11th)
Doncaster Pharmaceuticals	2.9	2.9	32.4	0.3	0.7 (10 <sup>th</sup> =)	2.16 (11th)	233.33 (8th)
Beachcourse Ltd	2.6	-	28.8	0.7	1.7 (9th)	5.90 (5th)	242.86 (7th)
G Pharma	0.9	0.7	9.9	0.2	0.4 (12th)	4.04 (9th)	200.00 (9th)
<b>Total</b>	<b>119.8</b>	-	<b>1,220.5</b>	<b>27.1</b>	<b>65.5</b>	(Average = 5.18)	(Average = 568.56)

Source: Companies House, April 2004.

**Table 5.6**  
**PD companies ranked by operating profit (2002)**

Company	Operating Profit	Operating Profit (2003)	Turnover (£m)	Fixed Assets (£m)	Gross Profit (£m)	Operating Profit/Turnover (%)	Operating Profit/Fixed Assets (%)
Waymade Healthcare Plc	16.8	-	270.0	6.9	33.9	6.22 (4th)	243.48 (6th)
Necessity Supplies Ltd	14.7	11.9	144.4	0.9	16.3	10.18 (2nd)	1,633.33 (2nd)
Jumbogate Ltd	7.9	-5.4	83.1	0.5	8.7	9.51 (3rd)	1,580.00 (3rd)
Intercare Distribution Ltd	6.4	-	143.1	1.0	12.7	4.47 (6th)	640.00 (4th)
Dowelhurst Ltd	5.9	7.9	193.8	1.1	9.9	3.04 (10th)	536.36 (5th)
Chemilines Ltd	5.8	4.4	47.8	0.3	6.8	12.13 (1st)	1,933.33 (1st)
Stephar (UK) Ltd	2.2	-	51.3	7.3	10.7	4.29 (7th)	30.14 (12th)
Lexon (UK) Ltd	2.0	1.7	47.5	3.2	4.8	4.21 (8th)	62.50 (10th)
Beachcourse Ltd	1.7	-	28.8	0.7	2.6	5.90 (5th)	242.86 (7th)
Interport Ltd	0.7	3.7	72.0	1.5	4.4	0.97 (12th)	46.67 (11th)
Doncaster Pharmaceuticals Ltd	0.7	0.6	32.4	0.3	2.9	2.16 (11th)	233.33 (8th)
G Pharma Ltd	0.4	0.2	9.9	0.2	0.9	4.04 (9th)	200.00 (9th)
Munro Wholesale Ltd	0.3	0.8	96.4	3.2	5.2	0.31 (13th)	9.38 (13th)
<b>Total</b>	<b>65.5</b>	<b>-</b>	<b>1,220.5</b>	<b>27.1</b>	<b>119.8</b>	Average = 5.18	(Average = 568.56)

Source: Companies House, April 2004.

**Table 5.7**  
**PD companies ranked by fixed assets (2002)**

Company	Fixed Assets (£m)	Fixed Assets (2003)	Turnover (£m)	Gross Profit (£m)	Operating Profit (£m)	Operating Profit/Turnover (%)	Operating Profit/Fixed Assets (%)
Stephar (UK) Ltd	7.3	-	53.1	10.7	2.2	4.29	30.14
Waymade Healthcare Plc	6.9	-	270.0	33.9	16.8	6.22	243.48
Lexon (UK) Ltd	3.2	3.7	47.5	4.8	2.0	4.21	62.50
Munro Wholesale Ltd	3.2	3.2	96.4	5.2	0.3	0.31	9.38
Interport Ltd	1.5	2.2	72.0	4.4	0.7	0.97	46.67
Dowelhurst Ltd	1.1	1.0	193.8	9.9	5.9	3.04	536.36
Intercare Distribution Ltd	1.0	-	143.1	12.7	6.4	4.47	640.00
Necessity Supplies Ltd	0.9	1.0	144.4	16.3	14.7	10.18	1,633.33
Beachcourse Ltd	0.7	-	28.8	2.6	1.7	5.90	242.86
Jumbogate Ltd	0.5	0.4	83.1	8.7	7.9	9.51	1,580.00
Chemilines Ltd	0.3	1.5	47.8	6.8	5.8	12.13	1,933.33
Doncaster Pharmaceuticals	0.3	0.4	32.4	2.9	0.7	2.16	233.33
G Pharma Ltd	0.2	n/a	9.9	0.9	0.4	4.04	200.00
<b>Total</b>	<b>3.2</b>	<b>-</b>	<b>1,220.5</b>	<b>119.8</b>	<b>65.5</b>	Average = 5.18	(Average = 568.56)

Source: Companies House, April 2004.

**Table 5.8**  
**Market share and profitability of full-line wholesalers, 1997/98**

Company	Turnover (£m)	Market share (%)	Return on sales	Operating profit as % of turnover
AAH	1,800	33.0	10.0	4.4
UniChem	1,500	28.0	-	2.9
Phoenix	484	9.0	12.0	2.3
Mawdsley-Brooks	82	1.5	7.3	1.7
East Anglian Pharmaceuticals	67	1.2	7.2	1.6
Graham Tatford	62	1.1	6.9	1.8
Sangers	37	0.7	6.8	1.9
Sants	31	0.6	7.7	1.3
F. Maltby & Sons	24	0.4	7.1	2.5
Norscott	19	0.4	11.0	3.4
Norchem	19	0.4	4.2	0.0
PIF Medical Supplies	16	0.3	6.1	2.2
Loveridge	8	0.1	23.0	1.1

Source: OXERA, July 2001.

**Table 5.9**  
**Comparison of full- and short-line wholesalers' turnover and profits 1992 -1999**

Full-line wholesalers									
	1992	1993	1994	1995	1996	1997	1998	1999	Av.
Turnover (£m)	1,379	1,479	2,969	3,255	3,449	3,943	7,595		
UK Turnover (£m)	1,367	1,462	2,950	3,229	3,429	3,939	7,573		
Gross Profit (%)	10	10	9	10	10	11	8		9
Operating Profit (%)	2	2	3	3	3	3	3		2
Return on Capital (%)	28	22	27	23	31	29	48		28
Short-line wholesalers									
Turnover (£m)	146	179	293	384	456	618	477	36	
UK Turnover (£m)	127	157	262	334	410	580	438	36	
Gross Profit (%)	10	10	9	8	10	12	11	25	9
Operating Profit (%)	4	4	4	4	5	7	4	10	4
Return on Capital (%)	44	39	48	33	38	53	40	65	40

Source: OXERA, July 2001.

**Table 5.10**  
***Proportion of PI licenses granted to non-BAEPD members***

<b>Month</b>	<b>Total number of PI licenses granted</b>	<b>% BAEPD members</b>	<b>% non-BAEPD members</b>
January 2003	206	19.4% (40)	80.5% (166)
June 2003	247	31.0% (76)	69.0% (171)
November 2003	249	38.1% (95)	61.9% (154)

*Source:* Author's own research.

## The Economic Impact of Parallel Trade

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### 6.1 Background

The financial and non-financial benefits of parallel trade to a country's health system and patients is wide-open to debate and, as expected, the debate falls between the key stakeholders, in particular drug manufacturers, parallel distributors and health insurance organisations. Parallel distributors maintain two arguments for parallel trade:

- i) It is argued that their industry promotes competition by forcing down the prices of their domestically-sourced counterparts;
- ii) It is further argued that through the parallel trade of pharmaceuticals, direct and indirect savings are realised, helping ever-increasing public healthcare expenditures in the EU.

Pharmaceutical manufacturers are naturally against the continuation of parallel trade in pharmaceuticals. The manufacturers' initial argument is that parallel trade undermines profitability and, consequently, harms investment in R&D and the potential for discovering new drug treatments. Several economic arguments have been put forward as to why parallel trade in pharmaceuticals is harmful to industry:

- i) No level playing field: manufacturers take all the risk in developing drugs and parallel distributors profit from the R&D of manufacturers;
- ii) Parallel trade undermines R&D by reducing overall industry profitability;
- iii) The EU is becoming increasingly unattractive for conducting business in because of the growth in parallel trade, which could cause job losses, cutbacks and industry re-location in the long-term.

These arguments will be further examined below in analysing the themes of three recent studies on parallel trade which were published by the Economic and Social Research Council (ESRC), the London School of Economics (LSE) and the York Health Economics Consortium (YHEC) respectively, and are relevant for the UK. Two further studies on parallel trade have been published and were identified but their focus was on Sweden and Finland and, therefore, of little relevance to the UK situation.

The UK market for parallel-sourced products has grown significantly between 1998 and 2002. Table 6.1 (p. 46) illustrates in pecuniary terms the extent of the growth in parallel trade between these years. In the UK, the amount of parallel-sourced pharmaceuticals has grown significantly and steadily from 1998-2002 in money terms and in market share, which has more than doubled since 1998 to 20 per cent, whereas the share of domestically-sourced pharmaceuticals has dropped by ten per cent. The value of domestically-sourced pharmaceuticals has also grown steadily, realising a 23 per cent increase between 1998-2002. Even so, this pales in comparison to the staggering rise in the value of parallel-sourced pharmaceuticals of 191 per cent from 1998-2002, which corresponds with the doubling of its market share over the same period.

### 6.2 Methodological issues

To date, we have identified five key studies on the effects of parallel trade on the pharmaceutical market in the EU. Two of these studies examined the impact of parallel trade in pharmaceuticals in the UK, but also Germany, Denmark, Sweden, the Netherlands and Norway (LSE and YHEC). The remaining three studies were more narrowly focused, analysing the impact of parallel trade in the UK (ESRC), Sweden and Finland respectively. We focused on the results produced by the three studies that were relevant for the UK (ESRC, LSE and YHEC). Their key methodological

points, objectives, research endpoints and key findings are detailed in the following paragraphs. Clearly, the three studies present methodological differences, which largely account for the differences in their specific results.<sup>1</sup>

The aim of the ESRC sponsored paper on 'Intellectual Property Rights and Parallel Trading in Pharmaceuticals' was to enhance the understanding of the impact of parallel trade on the welfare of consumers, purchasers and producers in the UK.<sup>2</sup> The objectives of this study were to:

- i) Understand the short-term incentive to engage in arbitrage trade and the longer-term impact on investment behaviour and the choice of the product mix;<sup>3</sup>
- ii) Calculate the impact of parallel trade on the UK economy and investigate the costs to UK consumers, pharmacies, the NHS, manufacturers and parallel traders;
- iii) Analyse how parallel trade impacts on therapeutic strategies.

The first objective was achieved through establishing behavioural models based on optimising agents to predict equilibrium outcomes. The second objective was difficult to achieve due to lack of adequate data. Therefore, the authors conducted a series of interviews to assess how parallel trade operated and how it was perceived by those who were affected by it.

In interviews, the ESRC study attempted to understand the views of three key interest groups, namely manufacturers, parallel distributors and pharmacists. In general, pharmacists only reported limited resistance to the use of parallel-distributed drugs by their patients. From the pharmacists' point of view, it was the large pharmacy chains using central purchasing who were more likely to employ parallel-distributed drugs. The only point of concern was that often the packaging was different. Expectedly, parallel distributors did not believe their activities had a negative effect on the manufacturers' R&D programmes while the manufacturers believed that governments should intervene to stop the practice or that the EU should act in a coordinated manner to do so.

Overall, the assessment of the study was that parallel trade has a negative impact on the UK economy, despite the short-term benefits for purchasers. The conclusion the authors reached, however, must be interpreted with caution as they believed that the impact of parallel trade will depend on the precise market conditions. However, the fact that the overall assessment of the impact of parallel trade is negative supports the conclusions of the LSE paper, published a few months earlier.

In January 2004 the LSE published 'The Economic Impact of Pharmaceutical Parallel Trade in European Union Member States: A Stakeholder Analysis'. This paper was supported by Johnson & Johnson and primarily aimed to provide a basis for assessing the future healthcare and industrial policy implications of parallel imports in six key European destination countries while also discussing the potential impact of parallel trade in a number of potential source countries in the EU.<sup>4</sup> The study further analysed whether or not parallel trade in pharmaceuticals offers any direct benefits to patients and indirect effects to both patients and payers, in terms of lower prices through competition and price convergence.

The Intercontinental Medical Statistics (IMS) database was used for all study countries. The research exercise focused on six product categories, i.e. proton pump inhibitors (PPIs), HMG CoA reductase inhibitors (statins), ACE I inhibitors, ACE II inhibitors, serotonin selective re-uptake inhibitors (SSRIs), and atypical anti-psychotics. A set of hypotheses was developed and these were tested in subsequent analysis. The hypotheses were derived from the economic and policy-related literature, both published and unpublished, theoretical/conceptual and empirical, and were as follows:

- i) From a theoretical standpoint (pharmaceutical) parallel trade results in significant re-distribution from low- to high-price countries in terms of lower prices in the latter. This is the standard 'arbitrage' hypothesis suggesting that 'price equalisation' across countries (subject to taking into account the transaction and other costs of arbitrage) is the result of conducting parallel trade, leading to improved (allocative) efficiency in the market place;
- ii) Assuming homogeneous products, standard economic theory postulates that (pharmaceutical) parallel trade results in (strong) price competition in destination countries, which

may lead to an overall price reduction in (pharmaceutical) prices, and which, in turn, has measurable and positive impact on payers and consumers;

- iii) If (price) competition is a result of parallel trade, then there should be price convergence leading to overall improvements for payers in terms of lower prices in the short term and enhanced market competition in the medium term;
- iv) Benefits to patients are significant and patient access to innovative, effective, but expensive medicines is improved. Patients benefit both directly, through reduced co-payments, and indirectly, through the savings passed on to them by health insurance organisations;
- v) Pharmaceutical parallel trade does not affect the ability of industry to operate profitably and does not harm its innovative capacity because it affects a small part of the market. Standard microeconomic theory also postulates that the loss to producer surplus forces producers (industry) to become more efficient. There are, however, suggestions that this may not apply to research-based industries such as pharmaceuticals.

The research exercise aimed to provide a stakeholder analysis of the impact of pharmaceutical parallel trade in qualitative as well as quantitative terms by examining the impact of parallel trade on both exporting (source) and importing (destination) countries. The key research endpoints were threefold:

- i) To evaluate the direct effects that arise from price differences between locally-sourced and PI pharmaceuticals in destination countries. The authors used the last year of the dataset (2002) to report on and focused mainly on drug list prices, while at the same time attempting to evaluate the impact of discounts in the UK and the Netherlands;
- ii) To evaluate the nature and extent of competition effects within destination countries, over the 1997-2002 period. The key endpoint here was to examine whether parallel trade leads to price competition and whether there is evidence that price competition between locally-sourced and PI products leads to downward price convergence;
- iii) To evaluate the nature and extent of likely price competition effects across (importing and exporting) countries and over time that would lead prices to converge, namely whether there is any foundation in the arbitrage hypothesis.

The York Health Economics Consortium study was commissioned by the European Association of Euro-Pharmaceutical Companies (EAEP) and published in May 2003. The study was designed to illustrate the benefits of parallel distribution and to whom those benefits accrue.<sup>5</sup> The study's focus was on the financial savings from products that are covered by a form of statutory health insurance. As in the previous case, a problem was the difficulty in accurately establishing the actual prices paid for pharmaceuticals. Any calculated savings were based on the difference between reimbursed prices for domestic and parallel-distributed products.<sup>6</sup> Datasets were taken from national statistics agencies or pharmacy bodies. IMS data provided a picture of the size, growth and penetration of the parallel trade market.

Discount data was especially hard to get access to in the UK, largely due to commercial sensitivities. Hospital purchasing agencies were reluctant to release information on the level of usage of parallel-distributed drugs in hospitals or about the savings that are gained from using such products. This was due to DoH pressure on purchasers to seek cost savings and pharmaceutical industry pressure on agencies not to issue contracts to parallel distributors.

### **6.3 Economic impact**

The results of all three outlined studies on the economic impact of parallel trade are outlined in Table 6.3 (p. 48). The ESRC study estimated that the saving to the UK health insurer was €360.1m, compared to €55.9m and €201.3m in the LSE and York studies respectively. Their calculations of the benefit to parallel distributors and the impact on industry were also higher than the other studies, at €720.3m for parallel distributors and €1.1bn impact on UK industry.

In comparison to these figures, the LSE study understated the levels of savings, benefits and impact. The study estimated that the total wholesale sales to pharmacists in 2002 (but not

hospitals) was €5.9 billion for the 19 drugs under consideration. From this, parallel traders took €648 million in gross profits and national health insurance funds or health services were able to claw back €100m in savings. The LSE study did not find any statistically significant evidence on intra-country price competition, despite the existence of several distributors active in each product market; neither was any statistically significant evidence found on price convergence across countries that would give credence to the arbitrage argument. Finally, pharmaceutical manufacturers may incur profit losses equivalent to the amount of the parallel import volume into the importing country times the price difference between exporting and importing country. This represents a loss to producer surplus, which is distributed to the above stakeholders.

The paper also examined the impact on source (exporting) countries quoting evidence on product shortages in some markets. Many EU countries are introducing or amending legislation to account for parallel trading activities on their territory. More importantly, there seems to be increased awareness about the extent of parallel exports in some traditionally low-price countries, notably Spain, France and Greece. Spain and France seem to be taking (or to have taken) action to account for the extent of parallel trade from their territory, but the measures introduced are strictly implicit and in accordance with European law. Spain introduced a royal decree requiring wholesalers to disclose the destination of the products they acquire from manufacturers. France has introduced a price notification procedure for major new products, allowing flexible pricing for innovative products. In Greece, concerns exist about the extent of parallel trade and the product shortages that have been noticed and which have been linked with its conduct.<sup>7</sup>

In contrast, traditionally high-price countries have mature policies in place to enable their health insurance systems to benefit somewhat from parallel importation of pharmaceuticals. This is the case particularly in the UK, but also in the Netherlands, Germany, and, to a lesser extent, Norway. Denmark and Sweden seem to be relying more on an information and substitution strategy rather than active promotion of PIs through financial incentives.<sup>8</sup>

Parallel distributors claim governments benefit greatly from the practice, but this has been contradicted by other independent evidence. One example is Medihealth's January trade in Nasonex. Medihealth bought the Schering spray from a French wholesaler for \$11.80 a bottle and English-language repackaging added another 37 cents. However, Medihealth sold the spray to British pharmacies for an average price of \$16.51, receiving a \$4.34 spread per bottle, or \$17,347 for the in-and-out shipment.<sup>9</sup> After a government levy, the pharmacist was able to take a \$1.48 trading profit, on top of a standard dispensing fee.

Parallel distributors act as profit maximisers, by observing and taking advantage of price differences for the same product between low- and high-price countries. These price differentials are not in principle observable by health insurance organisations. As a result, parallel distributors have no incentive in principle to offer health insurance organisations in destination countries significantly lower prices than locally-sourced products. In this respect, a given product market in a parallel importing country often resembles a duopoly. Understandably, parallel distributors incur certain costs to import a medicine into a certain country and these are both indirect and direct. The indirect costs relate to search in low-price countries, whereas the direct costs are associated with meeting the regulatory (safety) requirements. Another direct cost is the discount they provide to pharmacists where this is allowed. According to some sources this can range between 1.6 per cent and 23 per cent off list prices.

The York study confirmed that the UK market for parallel-distributed pharmaceuticals is one of the largest in Europe (€2,000 million in 2002). Overall, the study calculated a direct saving from parallel trade at €342 million. The authors further estimated that these savings were realised by the government in terms of lower hospital medicine prices and through the clawback mechanism applied to pharmacies (but, with a clawback average of ten per cent,<sup>10</sup> pharmacies may achieve significant profits). Overall, the total direct savings from the parallel trade of pharmaceutical products in 2002 were estimated as €342m in the UK. The study also found evidence that parallel imports have indirect competitive effects by forcing down the price of their domestically-sourced counterparts. Parallel trade also generates indirect savings by creating competition, where otherwise there is none, and thus forcing pharmaceutical manufacturers to

reduce the prices of domestically-sourced products. These indirect savings are difficult to quantify but they could be larger than the direct savings. The authors believed that the direct and indirect savings from the parallel trade of pharmaceuticals helped to slow down the rising public healthcare bill in many European countries.

**Table 6.1**  
**Domestic- and parallel-sourced pharmaceuticals (a)**  
**and Growth in domestic- and parallel-sourced pharmaceuticals (b)**

	1998		1999		2000		2001		2002	
(a)	£m	%	£m	%	£m	%	£m	%	£m	%
Domestically-sourced	4,420	90.5	4,665	88.1	4,754	86.4	5,232	82.9	5,454	80.2
Parallel-sourced	462	9.5	633	11.9	749	13.6	1,076	17.1	1,346	19.8
<b>Total</b>	<b>4,882</b>	<b>100.0</b>	<b>5,298</b>	<b>100.0</b>	<b>5,503</b>	<b>100.0</b>	<b>6,308</b>	<b>100.0</b>	<b>6,800</b>	<b>100.0</b>
	1998-1999		1999-2000		2000-2001		2001-2002		1998-2002	
(b)	%		%		%		%		%	
Growth in domestically-sourced	5.5		1.9		10.1		4.3		5.4 pa	
Growth in parallel-sourced	37.0		18.3		43.7		25.1		30.6 pa	
<b>Total</b>	<b>8.5</b>		<b>3.9</b>		<b>14.6</b>		<b>7.8</b>		<b>8.6 pa</b>	

Source: York Health Economics Consortium, May 2004.

**Table 6.2**  
**Overview features of studies on parallel trade relevant to the UK, 2004**

Study	ESRC	LSE	York Health Economics Consortium
Published	March 2004	January 2004	May 2003
Peer review	No	Yes	No
Data sources	Aggregate data on expenditure published by the DoH	IMS pharmaceutical sales database	Datasets were taken from independent sources such as national statistics agencies or pharmacy bodies. Where data was lacking, it was requested from parallel distributing companies
Sponsors	ESRC	J&J	EAEPCC
Methods	<p>The objectives were:</p> <ol style="list-style-type: none"> <li>1 To understand the nature of the problem from a theoretical perspective: assuming profit maximising behaviour by both manufacturers and parallel traders. We wanted to understand not just the short-term incentive to engage in arbitrage trade, but also the longer-term impact on investment behaviour and the choice of the product mix.</li> <li>2 To quantify the impact of parallel trade on the UK economy by looking at the benefits and costs to UK consumers, pharmacies, the NHS (i.e. indirectly taxpayers), manufacturers and parallel traders.</li> <li>3 To analyse how parallel trade might impact on the therapeutic strategies.</li> </ol> <p>The study conducted conventional economic analysis using behavioural models based on optimising agents to predict equilibrium outcomes. The authors also conducted face-to-face anonymous interviews with those affected by parallel trade and we have analysed some statistical data on prices of parallel-traded pharmaceuticals.</p>	<p>Stakeholder analysis and to attempt to quantify the extent of parallel trade and its economic impact on key stakeholders in selected countries. Research focused on the sales of nineteen high-volume medicines from six major drug classes over the period 1997-2002.</p> <p>-Survey of 12 EU member states on PT policies</p> <p>-Quantify the impact of PT by focusing on specific classes of products:</p> <ul style="list-style-type: none"> <li>• Statins</li> <li>• PPIs</li> <li>• SSRIs</li> <li>• Atypical antipsychotics</li> <li>• ACE I, ACE II inhibitors</li> </ul> <p>-To apportion any benefits to potential stakeholders</p> <p>-To assess the welfare impact of parallel trade</p> <ul style="list-style-type: none"> <li>• Comparable dataset across all sample countries and all products</li> <li>• PI prices and volumes available in Denmark, Germany, the Netherlands, Norway, Sweden &amp; the UK</li> <li>• Calculated intra-country price spread:(Porig- PPI) for all product presentations</li> <li>• Calculated inter-country price spread: (PPI - Porig*) for most popular product presentations</li> <li>• Savings to health insurance: the sum of direct (intra-country price spread) and indirect effects (e.g. medium-term competition); in absolute (€)and relative terms(%)</li> <li>• Revenues and profits to parallel importers: inter-price difference multiplied by PI volume in destination country; in absolute (€) and relative terms (%)</li> <li>• Direct effects only to pharmacies, excluding discounts</li> <li>• Consider cost-sharing structures when calculating impact on patients/consumers</li> </ul>	<p>The study conducted an analysis of savings and focused on the five largest pharmaceutical markets receiving parallel-sourced products in Europe:</p> <ul style="list-style-type: none"> <li>• UK</li> <li>• Germany</li> <li>• The Netherlands</li> <li>• Sweden</li> <li>• Denmark</li> </ul> <p>Statistical analysis was used to isolate competition effect by looking at the average price changes and price variance over time for both domestic and PD products.</p>

Source: Authors' compilations from the literature.

**Table 6.3**  
**Estimating the economic impact of parallel trade on stakeholders**

Study	ESRC, 2004	LSE, 2004	York Health Economics Consortium, 2003
Savings to health insurer	€360.1m	UK: €55.9m Germany: €17.7m Denmark: €3m Sweden: €3.7m Netherlands: €19.1m Norway: €0.56m	UK: €201.3m Germany: €194m Denmark: €9.1m (govt.) €6.6m (Insurance Comp.) Sweden: €36.6m (PBS) Netherlands: €27m
Total health insurer	€360.1 million	€100 million	€474.6 million
Benefits to patients	Not examined	UK: €0 Germany: €0 Denmark: €some Sweden: €some Netherlands: €0 Norway: €0	Not examined
Total patients	N/A	€ marginal but quantifiable by disease type	N/A + €10.1 (Co-payments in Sweden)
Benefits to pharmacy	Not examined	UK: positive but difficult to quantify Germany: €0 Denmark: €0 Sweden: €0 Netherlands: €6.3m Norway: €0.5m	UK: €141.2m Germany: n/a Denmark: n/a Sweden: n/a Netherlands: €4.6m
Total pharmacy	N/A	€6.9 million	€145.8 million
Benefits to PD	UK: €720.3m	UK: €469m Germany: €97.9m Denmark: €7.4m Sweden: €18.4m Netherlands: €43.1m Norway: €12.4m	Not examined
Total PD	€720.3 million	€648.4 million	N/A
Impact on industry	UK: €1.1 bn	UK: €524.9m Germany: €115.7m Denmark: €10.3m Sweden: €22.2m Netherlands: €68.8m Norway: €13.5m	Not examined
Total industry	€1.1 billion	€755.5 million	N/A

Source: Authors' compilations from the literature

## Overall Conclusions and Summary

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The principle of the free movement of goods within the European Union is key for the completion of the internal market, and parallel trade is, in theory, a means of evening price differences across member states. In pharmaceuticals, regulation at member state level prohibits the principle of arbitrage from working efficiently, and drug prices are not necessarily responsive to the pressures of parallel trade but only to the regulatory interventions that create them at member state level. In the previous sections we examined legislative, regulatory, institutional, market structure, and economic factors relating to the conduct of parallel trade in the UK. The key concluding points are summarised below.

### **7.1 Legislative issues**

As a result of numerous cases heard before the European Court of Justice (ECJ) since the late 1960s, a number of issues appear to have been resolved. In this context, specific policy implications of parallel trade include that:

- a) Parallel distributors do not have to repackage products, but may do so if they adhere to specific guidance, such as the protection of the condition of the product and the reputation of the trademark, giving the trademark owner notice, and stating on the product that it has been repackaged;
- b) Member states are required to afford simplified national registration rules for parallel importers such that if the health authorities of the destination country already possess the relevant information for the identical medicine, no further obligation is placed on the parallel importer;
- c) Provided the medicines are therapeutically identical, i.e. contain the same active ingredient in the same amount and same dosage form, there is no obligation for a parallel imported product to have a common origin to a domestic brand;
- d) Member states can disallow parallel imports for reasons of protecting public health and safety, including differences in product formulation and package size modifications that may mislead consumers (Article 30 of the EU Treaty);
- e) Manufacturers can manage their inventory so long as there is no outright ban on exports, no monitoring of the final destination of the product, and no agreement between undertakings (manufacturers & wholesalers);
- f) Important issues remain unresolved but are likely to be heard before the ECJ in the near future; most notably, these include (a) dual pricing, in the context of defining the geographical boundaries of a (national) market and (b) the abuse of dominant position and the criteria for defining it. Two pending cases, one on dual pricing (Spain) and one on abuse of dominant position (Greece), which will be heard by the ECJ in 2005 are likely to influence future policy direction on parallel trade, depending on the court's rulings;
- g) With ten new member states having joined the EU on 1 May 2004, it will also be necessary to observe how these will affect the future of parallel trade and how the EU will apply its governing principles, especially the principle of derogation.

### **7.2 Regulatory issues**

There are few hurdles before gaining marketing authorisation of parallel-imported pharmaceuticals through the centralised and the national regulatory procedures. Testing is not

needed, the product name can remain the same (although national regulatory authorities typically advise for the brand name prevailing in the member state of importation to be used), and the costs of the application are substantially lower than those of a new substance or a generic product. One key barrier to parallel importing of pharmaceuticals is the need for relabelling of the product and the insertion of a patient leaflet in the language of the destination member state. In some member states (e.g. the Netherlands), pharmacists can set up a wholesaling company and maximise their purchasing economies. The costs of obtaining a license for doing this does not appear to be a barrier.

There are regulatory controls for parallel-imported pharmaceuticals in each destination country. Regulatory approval is needed in each destination country, which comprises a short dossier and a fee payable to the regulatory authority of each country. At EU level and for products that have pan-European licensing through the EMEA centralised procedure, a pan-European parallel importation license can be obtained, subject to satisfaction of the regulator of safety and a fee payable.

Where centrally authorised medicinal products are concerned, the only changes that parallel distributors may introduce to the packaging of a medicinal product are those which are strictly necessary to market the product in the destination member state (e.g. use of different language version[s] of labelling and package leaflet; or change in the package size provided the proposed size falls within the scope of the EU MA). This is slightly different from the parallel importation of medicines authorised nationally because of differences between the marketing authorisation granted by the member state of origin and the one granted by the member state of destination.

The regulatory process is rigorous and this minimises the risk of counterfeit drugs. In the UK and over a period of eight years, only one such case was recorded. However, several violations regarding repackaging, relabelling, trademarks and inaccurate patient inserts have been reported by manufacturers to the relevant regulatory authorities. A significant number of these has been recorded in the UK. Of these, inaccuracies in patient inserts are probably the most important in terms of public health hazards, as they may provide out-of-date or even misleading information to patients and providers. Some violations have led to product recalls in some destination countries.

Parallel distributors are only allowed to procure products from a holder of a wholesale distribution authorisation in the source member state. The supplier is obliged to inform the parallel distributor of any recall activity originating with the supplier or earlier in the distribution chain including the original manufacturer that might involve products supplied to the parallel distributor. Such notifications must be handled within the parallel distributor's GMP system to confirm whether the affected product was actually received, trace its utilisation and initiate recall procedures as necessary, including contacting the local competent regulatory authority.

It is up to the trademark owner to check if the presentation after repackaging (should this occur) will not damage the reputation of the trademark owner. Problems have occurred in the past with the application of a sticker on top of the original trademark.

Parallel distributors are compliant with the national and EMEA procedures, although there have been cases where manufacturers have complained of improper handling of their products by parallel distributors.

### ***7.3 Institutional issues***

The way the distribution chain operates in the UK offers significant incentives to pharmacies to search for PI medicines and this process can also yield financial benefits to the NHS through the clawback.

The evidence suggests that, at least in principle, the clawback is a powerful mechanism that acts as an incentive for pharmacists to search for better deals when purchasing medicines from different sources. PDs can usually offer significant discounts over and above locally-sourced products and, in this case, the use of PI medicines is de facto promoted. In order to retain market share, locally-sourced products may need to be sold at the same discount off the list price, in a

so-called price equalisation deal. Of course, for all this to continue to happen, sufficient quantities of PI medicines need to be available in order to guarantee the sustainability of the market and, understandably, this may not always be the case.

The clawback applies to all pharmacies although chain pharmacies are excluded from the surveys that determine its extent. Theoretically, the objective of policy-makers is to extract the entire discount from pharmacies through the clawback, but this is not always happening, because discounts can be not only product-specific, but also pharmacy-specific. Elementary economic theory would suggest, for instance, that chain pharmacies may benefit more than single community pharmacies, simply because they have a larger purchasing power and, therefore, may be able to get better deals (discounts) from wholesalers or PDs. Out of all this, the NHS claws back a fixed (average) 10.44 per cent whereas pharmacies can retain the difference whatever this may be. It has also been suggested that discounts on generic products off the drug tariff can be even more significant. The entire process of pharmacy distribution raises questions about the economic efficiency of the system and the extent to which further savings can be achieved for the NHS. The recent pharmacy contract, withdrawing £300 million from distribution (pharmacy), highlights the fact that there may be significant 'slack' in the system.

Finally, the introduction of other institutional measures is likely to have an impact on the amplitude and extent of parallel imports into the UK. Key among them is the new PPRS. The agreed seven per cent price cut for all branded medicines with effect from 1 January 2005 is likely to have an adverse impact on the magnitude of parallel trade in the UK. The impact will also depend on how manufacturers select to deliver this price cut, i.e. whether this will be delivered as a seven per cent price reduction across the board, or as a cost neutral price modulation, where some prices decline more than seven per cent and others less than that figure.

#### **7.4 Market structure issues**

The UK market of parallel distributors is made up of 14 key companies who are members of, and organise, the British Association of European Pharmaceutical Distributors. The BAEPD is a non-profit organisation, promoting, protecting and developing the interests of its members who possess the appropriate licences granted by the Department of Health through MHRA for parallel distributing. In the UK, the amount of parallel-sourced pharmaceuticals has grown significantly and steadily from 1998-2002 in money terms and in market share, which has more than doubled since 1998 to 20 per cent, whereas the share of domestically-sourced pharmaceuticals has dropped by ten per cent.

The licence holders source prescription pharmaceuticals from any member state within the European Union (EU) where it is profitable to import from and distribute their products into the supply chain in the United Kingdom, either through retail pharmacies, dispensing general practitioners or hospitals and clinics. Pharmacies have an indirect incentive to procure more from parallel importers—the average clawback currently stands at 10.44 per cent. If pharmacies achieve a higher discount on this, then they can keep the difference.

#### **7.5 Economic impact**

The principle of the free movement of goods within the European Union is key for the completion of the internal market and parallel trade is, in theory, a means of evening price differences across member states. In pharmaceuticals, regulation at member state level prohibits the principle of arbitrage from working efficiently, and drug prices are not necessarily responsive to the pressures of parallel trade but only to the regulatory interventions that create them at member state level.

Statutory health insurance organisations in exporting (source) countries realise no benefits, whereas, from a conceptual perspective, their counterpart organisations in destination countries may benefit in three ways: first, in the case of price differentials in the list prices of locally-sourced and PI pharmaceuticals, the price difference accrues partly or in its entirety to them. In the Netherlands and Norway, the government involves pharmacists as direct agents to

maximise its financial benefits, by surrendering part of these to pharmacists. In Norway any likely financial benefits are equally split between the government and pharmacists, whereas in the Netherlands the pharmacist, until recently, retained one third of the price difference, surrendering the remainder to the government.

The second source of potential revenue to health insurance organisations is the 'clawback', which, according to the evidence presented, may arise either because of invisible discounts from wholesalers and parallel traders to pharmacists (UK, the Netherlands), or as a source of compulsion to pharmacists, operating in an environment of fixed wholesale and retail margins, to be able to procure from cheaper sources (Germany). Either way, health insurance wants to ensure that part of the pecuniary benefits accruing to pharmacists from more competitive purchasing, are in the form of lower reimbursement to them.

The third way through which health insurance might benefit is price competition, leading to (downward) price convergence in destination countries, although one cannot ascertain the extent to which this is occurring, and it is likely to be product-specific.

Pharmacists can also benefit in countries where pharmacy margins are not determined by regulation, and the UK is a prime example of this. In this case, benefits arise from individual negotiation, whereby pharmacists can negotiate discounts with parallel importers, making it profitable to stock and dispense a parallel-imported medicine that carries the same reimbursement price as a locally-sourced one.

The benefits to patients in destination countries theoretically accrue from the lower prices of PI drugs on the assumption that patients pay a significant proportion of their medication out-of-pocket. Reducing their overall medication costs will therefore improve access to essential medicines. In practice, however, European health systems, particularly in the UK, the Netherlands, Germany, Denmark and Sweden (and, perhaps, less so in Norway), provide comprehensive cover with low cost-sharing requirements. Where PI medicines have a price advantage over locally-sourced ones, the difference accrues to statutory health insurance, and patients therefore continue to be unaware of such price advantages.

The empirical evidence relevant to the UK finds significant benefits to parallel distributors, modest to moderate benefits to the NHS, mostly through the clawback, and no impact on patient access to care due to lower-priced medicines. The benefits to the NHS combined with those of parallel distributors are the sum of the loss to producer surplus. There is little or no evidence on price competition from parallel trade within the UK, and little evidence on price convergence between the UK and likely exporting countries.

## **Part II**

### **Pharmaceutical Parallel Trade in the UK: Patient Safety Issues and Proposals for Reform**



## **Editor's Introduction to Part II**

In Part I Panos Kanavos and Paul Holmes have demonstrated that the UK is a major parallel import destination. Parallel importation involves the legal repacking and reselling of genuine medicines. There are entrenched polar views on the subject. On the one hand we have importers, who argue that they are pursuing a legitimate business in a segmented free trade area. On the other hand, manufacturers see profits dented by parallel importing. Manufacturers and their associations argue that there is a serious knock-on effect on investment in the development of new drugs. Parallel traders refute this argument, and point to significant economic benefits brought to our NHS from their business.

Part II of this report enquires about only one potential spillover effect—the undermining of patient safety. With reference to evidence from Kanavos and Holmes and various stakeholders including patient organisations, pharmaceutical manufacturers and their representatives, we consider whether a high volume of parallel trade gives rise to legitimate patient safety/consumer protection concerns. Are parallel imports acceptable to patients? Is sustainability of supply a problem? Is there evidence of product tampering and of incorrect patient notes? And is product recall of goods easy? Parallel traders and their vocal associations refute suggestions that patient safety is threatened. They also argue that parallel importers are regulated in three different and complementary ways; more regulated than the manufacturers.

Section 2 contains submissions from two patient organisations, one from a company heavily reliant on parallel imports, namely Boots The Chemist, and another giving an academic perspective. Balancing these views, Section 3 summarises the patient safety concerns raised and asks whether they present a genuine threat. In an attempt to create solutions that would satisfy the vast majority of parallel traders, manufacturers and patients without erecting barriers to legal trade, Section 4 includes a number of policy proposals.

## Stakeholder Views on Parallel Trade

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### 1. Parallel Trade in Medicines: The Patient Perspective from Epilepsy Action

Sue Mitchell\*

The parallel trade in medication is damaging people's health and, at worse, putting lives at risk. Strong words, but when discussion of the parallel importing of medication seems to revolve primarily around money, the reality of patient experience goes unheard all too often.

Epilepsy is a chronic condition in which seizure control is almost totally dependent on medication. The term epilepsy covers recurrent seizures; some people will have a handful of seizures throughout their life, others will have several seizures a day. A seizure automatically means the loss of one's driving licence and the inconvenience that can come with that, including loss of employment for some. Seizures often result in injury, some minor, some requiring hospital treatment. Ultimately, a seizure can be fatal: 1,000 people in the UK die every year as a direct result of a seizure. Only 52 per cent of people have their seizures fully controlled by medication and even for those people control is very finely balanced.

Epilepsy medication has side-effects. The powerful drugs used act on the brain, often causing side-effects that can be correspondingly powerful. These side-effects can include problems with concentration, memory and cognition, sleepiness, weight gain and/or loss, mood changes, growth of body hair, loss of bone density and many others. As a result, people with epilepsy are understandably very concerned and cautious with regards to their medication.

#### ***Drug substitution***

As an organisation, Epilepsy Action is familiar with the issue of substituting one version of a drug with another. Over 1,200 people a day use our services and many have told us that, when taking a different version of their usual drug, they have experienced new or worse side-effects, or an increase in the number or severity of their seizures. Some people report experiencing their first seizure for years. Known as breakthrough seizures, these events can be a devastating blow to the person and their family. This change in seizure patterns and or side effects is commonly linked to switching to or from branded to generic, or from one generic to another.

There has been a slow and hard won acceptance that people with epilepsy should receive the same drug—be it branded or generic—every time they collect their medication; consistency of supply. Owing to a lack of funding for research in this area, the scientific evidence has been sparse and is only slowly growing. After a long battle the patients' voice is eventually having an impact. The National Institute for Clinical Excellence's draft guidelines, paragraph 1.7.7, state:

Different preparations may vary in bioavailability or have different pharmacokinetic profiles—careful consideration should be given to the potential for reduced effect or excessive side-effects before changing the formulation or brand of AEDs.

With progress being made on generic/branded switching, Epilepsy Action realised that the same problems were occurring as a result of parallel imports. We hear repeated assurances that all versions of a branded drug are identical. Interestingly, while many doctors, local chemists and parallel traders shout this loudly from the rooftops, the drug manufacturers themselves will not

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\* Communications Manager of Epilepsy Action and Editor of *Epilepsy Today*, a lay magazine for people with an interest in epilepsy. Epilepsy Action is the UK's leading member-led epilepsy organisation.

issue such a guarantee. We have been told that even the slightest difference in the non-active ingredients or in the storage or transport conditions makes them very wary of using the word 'identical'.

**Box 1. Comments from Respondents to Epilepsy Action's Questionnaire on Parallel Trade**

"My daughter was given a version[sic] produced in Greece and Spain. Five days later she had a major uncontrollable seizure and was in hospital for three days. She was unsettled for several weeks and had lots of smaller fits."

"My son's medication was suddenly changed to a Spanish version. I questioned this but was told there was no difference. After taking this version my son had constant stomach cramps, loss of appetite yet put on a lot of weight. After rejecting the drug, two stones in weight dropped off him and his appetite returned."

"My daughter's fits are uncontrolled—changes in medication and worries about side-effects are the last thing we need foisted on us!"

"My main concern was when we had mixed drugs from 2/3 countries put together in one box."

"My son had a bad case of breakthrough seizures by being given Spanish [drugs]. The pharmacist was not accepting what I told him."

"This research is long overdue. My son basically 'lost' a year at school due to being in a drug-induced 'fog' as a result of constantly adjusting to different brands of medication."

"I'm very glad you are looking into this—I know the foreign imports are cheaper, but surely patients' health is not worth gambling with, or am I living in a dream world? Every month I wait to see what I'm issued with."

"When my son was given a Spanish version he started to have partial seizures which stopped when he returned to his usual [drug]."

"Speaking to the pharmacist he was more interested in what it had cost him to get [the drug]..."

"My work and the stability of my family depends upon the success and stability of my anti-epileptic medication."

"I went through a phase of not wanting to go for my prescription for fear of not receiving the one I wanted."

"From being seizure-free, we have noticed seizures every day for about three months now. We have had Portuguese, Greek and Spanish versions during this period."

"It doesn't make me feel very safe that I had to ask for my prescription to be changed."

"My son was seizure-free for eight months, then had three seizures. As you can imagine he was devastated along with the rest of us. This issue needs addressing—it's messing with quality of life!"

Source: Epilepsy Action survey, 2004.

People have reported to Epilepsy Action that printed lists of ingredients have differed between UK and non-UK manufactured versions on some drugs, and one member even had his own laboratory test report produced, which identified different weights. The term 'identical' appears to be more flexible than its dictionary definition intends.

***Epilepsy Action research***

Having our case met with deaf ears by all apart from the drug manufacturers, Epilepsy Action decided to undertake some basic research. At the end of 2003, a random group of 1,851 members completed a questionnaire, based on their experiences over the previous 12 months.

When asked if they had been given their medication in different packaging or had been given a different version of their medication, 31 per cent said yes. We also asked if people had been offered medication in plain or unprinted packaging. Twenty-four per cent said yes.

Overall, 747 people had been given different versions of their usual medication or differently packaged medication. This phenomenon could entail branded/generic switching and parallel imports, either in parallel traders' packaging or packaging intended for other countries. We wanted to know whether these people had experienced any difference in their condition as a consequence. Of the 747 respondents, two per cent felt that their epilepsy had improved and five per cent were unsure, but a worrying 23 per cent felt that their epilepsy had become worse. This means that they had reported more seizures or more severe seizures than usual.

When we asked about the side-effects of these drugs compared to their usual drugs, one per cent said they had fewer side-effects, four per cent were not sure, but 32 per cent said they had more or different side-effects.

These are significant numbers: a third with worse or different side-effects and nearly a quarter with more frequent or more severe seizures. If we set these percentages against the 440,000 people with epilepsy in the UK, we can estimate that 101,200 people could be having avoidable extra seizures or more severe seizures. More or different side-effects could be affecting 140,800 people. The negative impact of this on those people's health and quality of life cannot be overstated.

Thankfully, when the people we surveyed spoke to their doctor or pharmacist about the problems they were experiencing, 51 per cent were given their usual version or packets by their doctor and 30 per cent by their pharmacist. However, 13 per cent of them were told by their doctor and 25 per cent by their pharmacist that 'they're all the same', while 10 per cent described their doctor as uninterested or dismissive.

We acknowledge that there will be those who refuse to accept our results, primarily because of a general reluctance to accept what patients say. We also acknowledge that our research will not satisfy those who demand 'scientific' research. Our response is that when people's health is being affected, whatever the cause, those people must be heard, and we would be delighted if someone with more funds than us would finance further and essential research.

### ***Patients' experiences***

Statistics are useful but they often fail to convey the depth or real nature of a problem. Box 1 includes just a few of the comments from the respondents to our questionnaire. The comments which are from patients and their relatives indicate that the issue of substituting different versions of a drug have several implications beyond those of more seizures and side-effects. People's trust in their health professionals and drugs is being damaged. Compliance is a known issue in most long-term medical conditions and for a patient to express fear regarding collecting a prescription can only be harmful. Stress can be a trigger for seizures, and the sense of anger and anxiety coming from many respondents could become an issue in itself.

### ***Parallel-imported drugs: the drugs 'pick 'n' mix'***

Epilepsy Action has had reports from people who have been given a mixture of drugs from two or three different countries in fulfilment of a single prescription. One woman telephoned to tell us she had been given a box of a drug called Epimaz from Israel. Another woman sent in the three packets she had collected from her chemist a few days before. One pack was her usual Tegretol Retard, the other two were printed in French and called Tegretol CR Divitabs. Even if these drugs are identical, these people believed that they had been given a totally different drug.

This latter experience is what we have come to call the pick 'n' mix approach to prescribing. An increasing number of people report being given a mixture of drugs, some brand names, some generic, some imported brand names, some branded drugs but supplied in parallel traders' own packaging or plain white boxes. At its worst, the pick 'n' mix approach results in people receiving different blister packs in a single plain white box. Even if the person escapes unscathed in terms

of their epilepsy, this causes confusion, anxiety, fear and a loss of trust in the doctor and pharmacist.

In all areas of health, the psychological impact of various issues must be considered. The placebo effect is well known and very powerful, and some have asked whether a similar 'reverse' placebo effect could be the cause of problems being blamed on parallel imports. Epilepsy Action acknowledges that this could play some part for some people. However, if the end result is a seizure, the underlying cause still needs to be addressed.

Several of the comments in Box 1 above come from parents. Many parents give their children the individual tablets to be sure that their son or daughter takes their medication correctly. In these circumstances, it is doubtful that the child has a high enough level of awareness for any 'reverse' placebo effect to result in extra seizures or side-effects. One parent rang to say that he had not noticed the fact that the new pack of tablets was made abroad. It was only when his daughter started to exhibit a severe tremor that he double-checked the medication. He demanded the UK version from the pharmacist and his daughter's health improved within 48 hours.

### ***Getting it right for patients***

Regardless of all the arguments claiming parallel imports do not present a problem for patients, the experience of the people who have to swallow the pills cannot and must not be denied. Medication should make people feel better not worse. One person, highly placed among European parallel traders, said he had never had a complaint from a patient. The reason for that is that most patients do not know the trade exists let alone how to complain about it.

Meetings about parallel trade tend to be dominated by discussion regarding who is making and losing money. With the exception of the wealthy, patients in the UK have no financial power. Could this be one of the reasons why the UK has so many parallel imports? There is also much discussion about imports cutting costs to the NHS, but who is counting the cost to patients? Who is counting the extra seizures, the extra visits to hospital, the lost jobs, the damaged social lives and the lost trust? Who will count the lost lives and bereaved families and who will hold their hands up when those families want to know who is to blame?

The first area of concern comes with the drug packaging. Even if we take the stance that the drugs are identical, the packaging certainly is not and often the drug name differs too. For example, the slow release version of the anti-epileptic drug Tegretol intended for the UK market is called Tegretol Retard; as we have seen above the French version of this drug is Divitabs. If we can go from Marathon to Snickers for the sake of a single European market, why can drug companies not follow the same route—naturally letting the patients know well in advance. (And while they are changing the names could they be more patient friendly—how many people happily show off their 'retard' pills?)

The UK government and the pharmaceutical industry spent years preparing for a change to secure tamper-proof patient packs. This system would have prevented many of the problems now being faced by patients. Unfortunately, the government decided to pull the plug on patient packs at the last minute. This was very bad news for patients and a golden opportunity missed.

The cheapest jar of jam or bottle of soft drink comes with tamper-proof packaging designed to protect consumers. But when it comes to the medication on which people's lives depend, there is no such protection. Packs are opened, cut up, mixed up, repackaged, relabelled—and the patient is expected to trust the pick 'n' mix result. The plain truth is that they do not. Patients are even losing trust in the people who prescribe and dispense them. This is very dangerous; as a society we should be doing everything possible to build and strengthen the trust between patient and health professional. Trust would be strengthened if regulations were introduced that make tamper proof packaging a legal requirement.

Associated with the practice of parallel traders unpacking and repacking the drugs before selling them on are the problems patients have in obtaining PILs (Patient Information Leaflets). The law requires that every patient is provided with a PIL every time they are given a pack of medication. Epilepsy Action's research revealed that 53 per cent of people receiving their drugs

in white or plain boxes did not receive a PIL. Of the 747 people who had been given different versions of their usual drug in the last year, 18 per cent were not given a PIL. Again, this system is failing patients.

No-one would argue that the NHS should not make savings where possible. However, the reality is that the NHS itself gains very little from parallel imports. It is the pharmacists and parallel traders that are making money. The pharmacist who buys the cheaper parallel import still claims the full agreed NHS price back. It is obvious to anyone that the more parallel imports they buy, the more money they make. The government claws back a token 10 per cent of the difference, but we must be under no illusion that the NHS is somehow saving a fortune—it is not.

Patients may not be consumers in the commercial sense, but in every other sense their status as consumers is beyond question. Why shouldn't the concept and rights of consumer choice be extended to them? In an ICM poll on parallel trading, 66 per cent thought it important that patients should have a choice. UK patients have no choice. Epilepsy Action regularly hears from people whose pharmacists refuse to provide anything other than the parallel import, blaming the government or the wholesaler. Many people with epilepsy cannot drive, so simply going to another chemist is not always possible. There are pharmacists who do listen to patient requests, but there are many that do not.

It is the patients' trust, confidence, safety and health that should be at the core of any regulations and activity to do with medication. If that trust is being ignored in favour of making or saving money, then our society and our health system has gone drastically wrong. Something needs to be done to enable the patient to be heard. Epilepsy Action struggles to be heard. If our research is unacceptable, who will pay for scientifically acceptable research?

This essay started with some straight talking. It will finish similarly. If parallel trading is here to stay, it must be safe and patient-centred. Patients should have the right of choice. Some patients, including those with epilepsy, should be guaranteed consistency of supply: namely the same drug, with the same name in the same tamper-proof package every time. These basic steps will improve people's health and quality of life as well as saving lives.

## **2. Parallel Trade from a Dispensing Chemist's Perspective**

**David Loudon\***

### ***Introduction***

Boots has a Wholesale Dealer's Licence for our central warehouse in Nottingham and we supply all parallel import (PI) versions of prescription only medicines (POMs) from that warehouse to our own pharmacies. We also have a buying team which sources PI's from a number of specialist importers. Boots is therefore a wholesaler of POMs and a pharmacy contractor with over 1,250 NHS pharmacies located throughout the UK.

The importing of PI's into the UK has been taking place for many years and is undertaken by most pharmacies, independents as well as multiples. This report is concerned principally with safety aspects of PI but before touching on that issue I would like to make a number of other observations.

### ***Economics of parallel trade in POMs***

There has been a great deal of debate recently on whether PI's make any savings to health services. The report published by the York Health Economics Consortium in May 2003, and sponsored by the European Association of Euro-Pharmaceutical Companies, suggested savings of €635 million in 2002 across five countries. IMS Global Consulting subsequently revised this figure to €421 million. A study by the London School of Economics, part funded by Johnson & Johnson, suggested that savings were lower and mostly went to parallel traders.

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\* Category Manager Dispensing Buying, for Boots The Chemists.

While it is possible to argue about the amount, there is no doubt that savings are made to the NHS through parallel trade. The current system of reimbursement to community pharmacy in the UK encourages pharmacists to buy at the lowest possible cost and most of this benefit is 'clawed back' by the DoH by means of a discount inquiry. Indeed, the DoH assumes a certain level of PI purchasing when setting the clawback rates for all pharmacies in the UK. Therefore, parallel trade in POMs makes savings in two ways. Firstly, it helps underpin the viability of community pharmacy in the UK. Secondly, it helps make savings to the NHS drugs bill.

### ***Activities of the major pharmaceutical manufacturers***

The major pharmaceutical manufacturers (the pharmacos) employ many different tactics to stop PI. Some examples are:

- i) *Litigation*: The pharmacos mount many legal cases against PI traders, usually about aspects of the repackaging/reboxing process. Although the pharmacos lose most of these cases, this puts extra pressure on the PI traders because they cannot match the pharmacos' legal budgets and they run the risk of having to pay substantial costs if they lose;
- ii) *Quotas*: Pharmacy contractors have found it more difficult to source PI recently, mainly due to the introduction of quota systems by the pharmacos, which limit the quantities of POMs available to each wholesaler in each EU country. The pharmacos claim they are trying to match more closely the supply to national demand but a consequence of this is to restrict any surplus available in low-cost countries for export to higher-cost countries like the UK. This happens in spite of further confirmation from the European Commission in a statement dated January 2004 that parallel trade in pharmaceuticals is legal and should not be restricted;
- iii) *Pricing*: Pharmacos will sometimes reduce the standard UK trade price of a product to below the market cost price of the PI equivalent, and the recent PPRS price reductions provide some examples of this.

### ***Patient safety***

- i) *General Perspective*: Parallel trade is carefully regulated in the UK by the MHRA and has a good patient safety record. In spite of this, there appears to be a growth in subjective opinion, suggesting that this may not be the case in the future. A couple of examples occurred in the report published in May 2004 on parallel trade in medicines by the Social Market Foundation. Firstly, IMS are quoted as saying that a medicine can change hands up to 20 or 30 times through parallel trade. The person concerned at IMS has subsequently informed me that this was a throw-away remark which amounted to 'hyperbole'.<sup>1</sup> Secondly, the author of the SMF publication suggests links between parallel trade and counterfeit medicines entering the EU, when in fact there is no evidence to substantiate this claim. A great deal of this scaremongering seems to be linked to the recent admittance to the EU of countries from Eastern Europe, when in fact derogations inserted into the Accession Treaty signed by the ten new accession countries effectively limits parallel trade for an indefinite period to a very small number of products;
- ii) *Boots' Experience*: We have been providing PIs to our pharmacies for many years and would not risk providing POMs which were in any way sub-standard or would put the safety of our patients at risk. We supply approximately 600,000 packs of PI per month to our pharmacies and can find only five instances since the start of 2004 where there have been difficulties. These were all relatively minor issues involving either labelling errors or wrong pack sizes and none of them posed a significant risk to patient safety. For example, we recently took delivery of a small quantity of a particular pack of tablets which had the correct product packed in the correct carton but were incorrectly labelled as capsules on the blister inside the carton. The batch in question was recalled from our pharmacies and returned to our supplier;

- iii) *Role of the Internet*: It is important to distinguish between carefully regulated, legitimate parallel trade in POMs, which is restricted to within the EU countries, and individuals sourcing medicines themselves from non-EU countries via the internet. The latter could clearly incur patient safety risks which do not apply to true parallel trade.

### **Conclusion**

We believe that parallel trade in POMs is a carefully regulated, legal activity which contributes to savings in the NHS drugs bill, helps underpin the viability of community pharmacy in the UK and poses no risk to patient safety. Our own experience of parallel trade, as the pharmacy chain with the largest NHS dispensing business in the UK, has been very positive and we are dismayed by recent attempts to alarm patients. We appreciate the opportunity to contribute further to this debate.

### **3. All is Not What it Seems—Parallel Trade from a Patient Organisation Perspective**

**Jim Thomson\***

Early in 2004 someone in Depression Alliance purchased 100 Amitriptyline tablets. Amitriptyline is a tricyclic antidepressant and that quantity is sufficient to kill several times over if taken in overdose. Even at common prescription levels, there are several issues that need to be considered when prescribing or taking such a medicine. The buyer had no consultation, there was no prescription and therefore no indication of what dosage would be advisable. However, she did have a credit card and access to the internet. A Google search yielded hundreds of online pharmacies willing to sell her the medicine—many appeared to be UK-based but in reality were not—and after submitting the order, the package duly arrived. It was stamped with the buyer's name, address and mobile phone number and the words 'Medical Supplies'.

Depression Alliance would rather that it was not possible to order powerful prescription medicines much as one orders a book from Amazon. Given the stigma and discrimination surrounding mental illness, it is extremely difficult to persuade people when it is time to seek professional help. We would rather patients were able to visit their GP, confident in the knowledge that whatever the outcome for their health, they certainly were not risking their future employment prospects, ability to travel or to obtain insurance or other financial services.

Against a backdrop of fear and denial, it is conversely relatively easy to self-diagnose, for example, depression. Depression Alliance, through its website and literature, provides a great deal of information that would contribute to an educated guess at a diagnosis of depression. Faced with the prospect of having a mental illness on their records, it is easy to see why some patients would be tempted to self-prescribe.

Depression Alliance is so concerned that we approached several of our contacts in the pharmaceutical industry to ask what was being done to regulate such activity. We were flabbergasted by what we found. It seems that not only does the online buyer effectively enter a lottery when they make a purchase, but so does the patient walking into the High Street pharmacy clutching their prescription. This Civitas report will make worrying reading but perhaps the most worrying thing is that for those of us who have been looking at the world of parallel imports and online pharmacies, it holds no surprises. Parallel importation is a world of profit without re-investment in research, of profit without responsibility for patient welfare, and of profit without a conscience.

One of Britain's most popular pastimes is DIY. A bit of plumbing, decorating or furniture-making may be all well and good but when DIY extends to medical interventions, we think the

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\* Chief Executive of Depression Alliance. A user-focused organisation, Depression Alliance works to relieve and to prevent this treatable condition by providing information and support. Depression Alliance works to improve the service provision for those affected by depression and campaigns to raise awareness amongst the general public about the realities of this severe and enduring illness.

trend has gone too far. We bought enough Amitryptiline to kill—with no questions asked. Doing so was easier than buying a similar amount of Paracetamol from the local chemist. That cannot be right.

### ***Editor's Note***

The concerns Jim Thomson presents in this brief contribution relate to self-diagnosis and the purchase and supply of medicines on the internet. As David Loudon points out in his contribution above, readers should note the distinction between the unmonitored use of drugs purchased on the web, and fully medically monitored use of parallel imported products. Only the latter is relevant to this pamphlet, related as is to products available within the UK legitimate supply chain; nevertheless parallel trade may have implications such as those raised by Sue Mitchell of Epilepsy Action, namely problems of consistency of supply, and of confidence in medication which in turn is closely related to compliance.

However, patient web-purchasing is not connected with parallel trade, as was emphatically underlined by EAEPC Secretary General Donald MacArthur during the Civitas conference on patient safety and parallel trade, held at Portcullis House on 24 June 2004, at which Jim Thomson made the points above.

While we cannot ignore the issues raised by Jim Thomson, unless and until stricter regulation of web-based pharmaceutical purchasing is introduced, the *caveat emptor* doctrine seems appropriate for online pharmacy. Nevertheless, the buyer beware position leaves a difficult policy conundrum: how should vulnerable patients with depression, in an environment of stigma, be protected from making decisions that under normal circumstances the reasonable 'man on the Clapham omnibus' would not make? Tackling the stigmatisation of depression as an illness is perhaps most important; in the meantime there is a danger that the distinction between counterfeiting, parallel trade and online pharmacy will be muddled. As a result, many of the serious problems thrown up by each may not be addressed.

## **The Parallel Importing of Medicines in Europe: Private Concerns and Public Interests**

**David Taylor\***

Most public discussion about the parallel importing (or in US parlance 're-importation') of medicines in the EU illustrates the fact that it is difficult to communicate in balanced ways about complex issues involving conflicting policy goals. There is a natural tendency to simplify and to focus on what for each particular group of 'stakeholders' are 'key' facts. But all too often this approach leads to an unsatisfactory debate, which is partisan and confusing. This serves to prevent rather than promote the understanding and protection of the public's best interests.

In the European context the proponents of PIs argue that if cheaper forms of a given medicine are available in one part of the single EU market as opposed to another, it must make sense for pharmacists and other care providers to purchase at the lower cost. This will—PI advocates suggest—allow other forms of care or service to be afforded, or taxes and fees to be lower than otherwise would be the case.

Against this, PI opponents say that its savings are exaggerated and that its costs, not only to innovative companies but also to the wider public, outweigh its benefits. Permitting parallel

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\* David Taylor is an NHS Trust chairman. His university position as Professor of Pharmaceutical and Public Health Policy in the School of Pharmacy, University of London, is publicly funded, and he receives no personal income from consultancy. His research activities are funded via grants and fees paid via the School of Pharmacy, University of London, by a range of public, voluntary and private sector organisations with interests in the pharmaceutical and wider health care sector.

importing may, they believe, raise the risk of harm resulting from causes such as medication errors associated with factors like patients not recognising their treatments and the problems of drug counterfeiting. Although the latter are most acute in less developed countries, where vulnerable populations are often open to exploitation and hazard on a large scale, they should not be ignored in Europe and the US.<sup>2</sup> Recent work for the Council of Europe has emphasised this point.<sup>3</sup>

Critics of PI have long warned that parallel trade introduces a vehicle for counterfeits to enter the legitimate supply chain. In the autumn of 2004 PI Cialis tablets supplied in Holland were found to be counterfeit: their route of entry into the legitimate chain was confirmed as having been parallel trade.

However, the 'real world' is more complex than simplistic claims about parallel importing being unequivocally harmful or beneficial may imply. The analysis offered by Kanavos and Holmes in this volume indicates that in the EU pharmaceutical parallel importing has (to date at least) taken place without significantly undermining standards of patient care, or the integrity of the pharmaceutical supply chain. David Loudon's authoritative description of Boots' approach to the supply of PIs drives home this point. However, the assumption that parallel importing is economically beneficial to countries such as the UK is not convincingly made. Although mistakes are made in medicines repackaging by parallel traders, Boots has always been able to correct them before they put patients at risk.

In fact, the research available offers fairly robust evidence that the savings to the public purse achieved as a result of PI use have been small compared with total European drug outlays. They have also been significantly less than the income losses as a result incurred by research based pharmaceutical companies and their subsidiaries located in this country.

Even discounting all harm caused to patients (and partly hidden costs such as those associated with the purchasing of PIs by NHS pharmacists, and the resources needed to maintain complex regulatory safeguards over product quality) the impact of parallel importing on UK pharmaceutical industry interests has been significant. This factor was one of the reasons why an independent ESRC-funded group led by Professor Stefan Szymanski of Imperial College recently found its net UK value to be negative.<sup>4</sup>

The long-term balance of gain and loss for EU nations that export PI products is also less certain than might at first appear. For instance, supply problems can occur when medicines are diverted away from domestic to external markets. Over time a shift to more standardised medicines pricing across EU states might also disadvantage countries which have traditionally set lower than average drug prices in their home markets, while still enjoying full access to the fruits of modern research.

### ***Europe's long-term goals***

Such observations need to be informed by an appreciation of the economics of pharmaceutical development and supply, and the political imperatives underpinning the creation of the European single market.

Normally, the average selling price of a patented medicine is many times the cost of its basic ingredients. This is because 'sunk' costs associated with research, manufacturing and marketing must be recouped within a narrow window of time. Patented medicine prices must also be high enough to allow adequate returns to investment (and/or attract further investment for the future) to be generated before generic competition ensues. As recent events surrounding medicines such as Vioxx demonstrate, the pharmaceutical industry faces high levels of commercial risk. Investment returns should compensate for this fact.

But the marginal production cost of a new medicine will by definition be much closer to its ingredient cost, and its eventual generic price. Just making one additional batch of a product will typically require very little extra spending. Many economists would argue that in such circumstances, and particularly when health or similarly vital 'customer' concerns are at stake, better-off communities ought to pay more per unit of consumption than poorer ones. Provided

that losses are not incurred as a result of any one sale, strategies based on this type of price discrimination ('Ramsay pricing') help maximise both private returns and the welfare of all sections of the public.

However, the free movement of patented medicines between richer and poorer EU nations today tends to obviate this option. The European situation is also complicated by the fact that formal (as opposed to voluntarily discounted) medicine price differences within the Union are often in effect imposed by member state-based regulators, rather than resulting from the freely made decisions of the innovators holding intellectual property rights for the products concerned.

Agencies such as the European Commission may, it can be conjectured, wish to see a gradual removal of national level controls over all sectors of the European economy, and the emergence of stronger pan-European regulations and institutions. The establishment of a single European 'free market' could be regarded as key step towards achieving the long-term political goal of establishing more comprehensive central competencies in fields such as the health sector.

The phenomenon of pharmaceutical parallel importing within the EU can be seen in this context. It is not purely associated with a movement towards freedom of trade, away from local protectionism towards greater efficiency. It is arguably more an artefact (or even 'side effect') resulting from competition for bureaucratic power and political legitimacy between regulatory and governmental interests in the EU member states and their counterparts in Brussels, the ultimate costs and benefits of which remain uncertain. In such circumstances it is in the overall public's interest to promote awareness of its possible hazards, to seek to ensure that European industry's vital organs—which include its research-based pharmaceutical sector—do not suffer irretrievable long-term damage.

### ***Global lessons?***

In conclusion, the evidence offered by the contributors to this Civitas report suggests that EU policy makers could, if they wish to, continue to permit the parallel trading of pharmaceutical goods within the expanding EU single market for an indefinite period. Challenges associated with the entry of Eastern European member states will probably make it harder in future to ensure drug quality and safety, and prevent crimes such as medicine counterfeiting. So too may an increased use of the internet for medicines purchasing, especially in the absence of high quality publicly funded health services. Yet the fact remains that the European record since the 1970s indicates that, if enough effort and money were invested in regulating parallel trading in medicines in the expanded EU, it could be conducted ethically and—at least in the great majority of cases—safely.

The positive achievements of the regulators and companies involved in legal parallel trading in the EU deserve fair recognition. However, policy questions remaining to be answered include:

- i) what relevance does the European example have for the wider world?
- ii) what in future will be the overall balance of the European public's interest in relation to the trading of locally-priced patented medicines across its internal borders?

Neither can be answered simply. In relation to the first question, the European Union is in many ways a special case. What works in the EU would not necessarily be viable in the US, or in less advantaged regions of the world. Indeed, if improving global health and reducing worldwide health inequalities is taken to be one of the most important challenges of the twenty-first century, Europe's experience with promoting medicines parallel importing is largely irrelevant. It will arguably be much more important to find ways of better controlling the international movement of pharmaceutical goods, both to protect the integrity of their supply and to allow poorer populations to benefit selectively from the lowest possible prices.

With regard to direct European interests, it may well be concluded that the most important concerns at stake relate to maintaining and further developing knowledge-based industries, and creating beneficial new health and other technologies. The short-term value of making even minor savings in pharmaceutical/health service outlays should not be ignored, especially in

communities which do not see themselves as direct beneficiaries of more sophisticated forms of research-based industrial activity. Nevertheless, maintaining the long-term living standards of Europeans demands adequate investment in just such forms of enterprise. Informed public discussion of the positive and negative aspects of parallel trading of medicines in the EU ought (whatever the private interests of entrepreneurs, taxpayers and social security recipients) to serve, in the final analysis, to highlight this economic reality.

## **Evidence of Patient Safety Concerns**

### **Benedict Irvine**

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This section of Part II summarises and briefly discusses potential patient safety concerns. The evidence presented comes from patient organisations, manufacturers and their pan-European representative organisation, the European Federation of Pharmaceutical Industries and Associations (EFPIA). The parallel importers and their representative associations dispute the validity and import of this material. We do not examine trademark issues (repackaging/labelling and de-branding/co-branding), which, though they have been the subject of much case work in the ECJ, do not impact upon patient safety.

Table 1 (p. 68) shows evidence directly collected from manufacturers and their national and European associations. The patient safety issue, specific manufacturer concerns and likely parallel distributor response are included. Meanwhile Table 2 (p. 69) shows concerns raised by patient organisations involved in this project.

Are any of the concerns set out in Tables 1 and 2 legitimate? Or are the sources scare-mongering? In Part I of this report, Panos Kanavos and Paul Holmes point to many repackaging problems (p. 24) that have been discovered, and which to varying degrees of seriousness amount to breaches of regulations. But Kanavos and Holmes also question whether patient safety is threatened by parallel trade.

#### ***The concerns of manufacturers***

Some, though not all, manufacturers consider that the repackaging objectively required if medicines are to be imported into the UK might not take place under ideal GMP conditions and therefore that repackaging may jeopardise patient safety; the list of errors made is reflected in Table 1. However, it is possible that the EAEPC trade association secretary general Don MacArthur's cost-saving rationale for parallel trade belies what may be the primary concern of manufacturers—namely, loss of profits. This is an understandable position, which naturally leads to the question: what are the consequences of lost profits on subsequent research and development expenditure? Is there a genuine link between parallel trade and research and development expenditure? And what should be the future role of governmental price and reimbursement regime regulation—a primary cause of price differentials?

The pharmaceutical companies also express three other fears. The first concerns lack of control of their products within the supply chain, a situation which has led to product shortages in certain countries of origin. Associated with this loss of control is the fear on the part of some companies that parallel trade may become a vehicle for counterfeit products to enter the legitimate supply chain. Their second fear assumes that if such counterfeits did enter the supply chain, the reputation and profitability of the manufacturer concerned would be severely damaged. However, months of research yielded no evidence of European parallel trade acting as a gateway for counterfeit products. The third fear concerns product recall processes and the impact of repackaging on traceability of medicines.

#### ***The traders' position***

Europe's importers, and those companies like Boots The Chemist which source products from them, strongly refute any suggestion that patient safety is threatened. They point out that parallel

**Table 1**  
**Manufacturers' Evidence Summary**

Issue	Manufacturers' Concern/Implications	Importers' Possible Response
<b>Medicines Supply Problems</b>		
Inconsistency of supply in country of origin	Shortages for patients; loss of income	Manufacturers could supply sufficient product
<b>Repackaging Problems<sup>1</sup></b>		
Leaflet out-of-date	Missing information; side effects, warnings, safety restrictions not shown	Manufacturer/regulatory authority could have notified of change; were simply submitting this evidence for trademark purposes
Leaflet has conflicting info (with other packing) or missing info	Confusion/safety	MHRA has approved as is
Size of font on PIL/package	Illegible to patients; confusion/safety	MHRA has approved as is
Mismatch between batch numbers	Difficulty of product recall	Qualified persons did not check as were submitting this evidence for trademark purposes
Mismatch between expiry dates	Danger to health/ineffective product. Difficulty in product recall across Europe.	Qualified persons did not check as were submitting this evidence for trademark purposes
Expired product	Danger to health/ineffective product	Submitting this evidence for trademark purposes
Fading of expiry date on new box	Danger to health/ineffective product	Acknowledge problem
Translated calendar on blisters not matching that on PIL	Patient confusion	Not serious
Over-labelling of blister packs peeling off.	Patient confusion	N/A
Cutting of blisters <sup>2</sup>	Difficulty of product recall/Confusion/safety	This is permitted
Missing info on labelling	Safety	MHRA has approved as is
Wrong form of delivery/no brand licence	No licence for distribution	N/A

Notes:

- 1 Those discovered in course of market authorisation notification to manufacturer process.
- 2 Blisters of ten cut into 8+2 to make boxes of 28. What happens to the off-cuts? Perhaps one box full of twos is made up? In theory, if expiry dates and batch numbers were the same and if blisters were undamaged, there is no patient safety problem. But is it likely that batch numbers would be the same? And in any case, there is a real danger of damaging the blister seals.

Source: Pharmaceutical manufacturers; EFPIA

importers are regulated in three different and complementary ways. First, every parallel-traded product must have an abbreviated marketing authorisation. Secondly, every parallel importer that does repackaging/relabelling has to have a manufacturer's authorisation (and employ a legally responsible EU Qualified Person in the same way as other manufacturers). Thirdly, if they supply pharmacies they have to have a wholesale dealer's authorisation. Don MacArthur argues: 'As far as I am aware there is zero evidence that patient care has been harmed by parallel trade in any way—to the contrary, it improves patient care by making expensive medicines more affordable to payers—and as for counterfeits there is not one confirmed case anywhere in Europe of a counterfeit drug reaching a patient as parallel trade in over 20 years.'<sup>1</sup> On the subject of recalls, the EAEPIC argues, 'our members have shown they can perform these just as competently

as manufacturers.’ MacArthur continues: ‘we have to be whiter than white, otherwise Big Pharma would come down on us like a ton of bricks.’<sup>2</sup> The contribution from David Loudon of Boots The Chemist clearly echoes these sentiments. Like the EAEP, Loudon’s perspectives are driven by sound commercial logic. Questions regarding patient safety might be legitimate, but remain unsatisfactorily proven. Thus, until the brand industry comes up with a greater body of evidence proving that parallel trade can affect patient care, importers’ cries of defamatory scaremongering have weight. However, in the course of editing this pamphlet, two drug recalls by the MHRA perhaps point to such evidence having been found.<sup>3</sup> An MHRA inquiry into the matter is ongoing, but comment from Dr Richard Barker, Director General of the ABPI, suggests such occurrences would not occur if parallel trade did not exist:

This incident highlights the need for the greatest vigilance and scrutiny, especially when medicines are introduced into the system other than from their original manufacturers. The best protection against counterfeiting is to ensure that the products bought are those supplied by the authentic manufacturer. Only then can the industry feel confident that its products are reaching patients in the same condition as they left the factory, and that patients are receiving medication that they can trust absolutely.<sup>4</sup>

**Table 2**  
**Patient Organisation Concerns**

<b>Issue</b>	<b>Patient Organisation Concern/Implications</b>	<b>Possible Importer Response</b>
Lack of medication continuity (Epilepsy Action and Depression Alliance)	Could be cause for concern/create confusion in many patients; may lead to poor compliance/concordance	Not related to parallel trade
Repackaging errors (see above)	Missing PIL, missing information; side effects, warnings, safety restrictions not shown. Danger to health/ineffective product. Difficulty in product recall across Europe	There is no hard evidence of such errors being caused by parallel importing
Missing or incorrect PIL	Missing information; side effects, warnings, safety restrictions not shown	Not known

Source: Author’s research; Epilepsy Action; Depression Alliance.

### ***Full-line wholesalers versus short-line traders***

Readers should note that there is an important distinction between actors dealing with parallel-traded products. As Niall Maclean spells out in his recent Social Market Foundation pamphlet, ‘normal full-line wholesalers provide a community service, in that they operate 24 hours a day, carry all commercially available pharmaceutical products, and ensure availability at least twice a day within a certain proximity to the pharmacist.’<sup>5</sup> The short-line wholesalers do not have such responsibilities. We have seen that some 55 per cent of parallel trade to the UK is in only 12 products. Full-line ‘wholesalers have claimed that by cherry-picking the most profitable products parallel trade impacts significantly on their business model, thus potentially jeopardising their social function.’<sup>6</sup>

### ***The regulator’s perspective***

Civitas asked the MHRA to respond to some of the potential patient safety concerns highlighted by manufacturers (Table 1). Regarding product recalls, the MHRA representative we contacted did not consider parallel trade a safety threat.<sup>7</sup> Manufacturers and parallel distributors are required to maintain records to enable effective recall throughout the supply chain. The marketing authorisation (product licence) holder (the MAH) is responsible for effecting product recalls. That MAH must notify wholesalers, who in turn are bound by good distribution practice

(GDP) to inform their customers, including other wholesalers, whether or not in the same country. It does not matter in which EU country the product originated, as GDP requirements apply throughout the EU. The MHRA informs other countries' authorities of Class I (action within 24 hours) and relevant Class II (action within 48 hours) recalls via the Rapid Alert fax system.<sup>8</sup>

Civitas also asked how a recall could occur in one country, but not others. Was this a case of regulatory failure? The MHRA representative stated that MHRA has good relations with other EU countries, so lack of communication is not a problem. A typical example of single-country recall might arise where the problem affects only one language leaflet. For example, if the Spanish patient information leaflet was incorrect, but the English one provided in the UK PLPI product was correct, the MAH would only need to alert customers receiving the product with the Spanish leaflet and the UK parallel-imported product would not be affected (although would be informed because they receive the product with the incorrect Spanish leaflet and replace it with the correct UK leaflet).<sup>9</sup>

### ***The concerns of patient organisations***

Back in 2001, the UK Consumers' Association journal, *Consumer Policy Review*, published an article by Don MacArthur which supported parallel trade, arguing that it was of benefit to the NHS and patients and should thus be supported.<sup>10</sup> Those patient organisations involved with this project hold the opposite view, but cannot claim without *caveat* that their particular concerns are directly related to parallel trade. Depression Alliance is concerned about unregulated access to medicines through mail order exacerbated by online pharmacies. Counterfeit products are a threat in that arena, but perhaps the more worrying issue is that patients are self-diagnosing and cutting out the vital doctor-patient relationship upon which EU health systems are all based. Such a relationship better enables appropriate prescription, taking into account relevant patient medical history, co-medication, also allows for monitoring of compliance and efficacy, and usually involves follow-up. Prescriptions from GPs or specialists are typically either dispensed within a hospital or a community pharmacy, which in turn will have means of contacting those to whom they dispense medicines. None of these precautions are guaranteed when purchasing over the web, although the web often can obviate asymmetry of information between patients and healthcare providers.

Meanwhile Epilepsy Action's concerns are legitimate, but could be said to focus primarily on continuity of medication. That is to say, patients should continue to receive the same treatment, and should not accept generic substitutes or parallel-imported products, despite the fact that the latter ought to be identical. Sue Mitchell cites a survey, which though not scientifically flawless, nevertheless revealed worrying results. Her calls for further research should be taken seriously.

The potential for confusion in the face of a product with a different name and in a different box seems serious. For many patients—including the most vulnerable such as those with Alzheimer's—uncertainty and distress must be sources of concern.

Neither of the patient organisations involved in this project expressed concerns about product recall processes.

## Proposals for Reform

### Benedict Irvine

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The repackaging errors, patient confusion and uncertainty, alongside shortages of supply in a number of countries, summarised in Section 3, give cause for concern. These proposals attempt to tread the fine line between raising legitimate patient safety concerns and those that are less credible. Reference to counterfeiting is included only as a *potential future threat* to the supply chain. Nevertheless, some of the following proposals might have a desirable preventive effect.

The knee-jerk solution to a perceived threat to patient safety would be to ban parallel trading in pharmaceuticals. This might be justified by the argument that although the trade is in accordance with EU law, the role of national government in setting pharmaceutical prices and reimbursement mechanisms nullifies the advantages of the free movement of goods and gives rise to important welfare effects. Although the banning of re-importation is a solution that still has currency in the US, it is certainly one of the least likely solutions in a UK and European context as so many key players, including a number of governments, are supportive of the trade. Meanwhile the European Commission and the ECJ place great emphasis on the freedom of movement of goods and the promotion of competition (Articles 28-30, 81 and 82 EC Treaty).<sup>1</sup> So what other solutions might be more acceptable? Is there a win-win solution that would satisfy the European Commission, the brand industry, the vast majority of parallel traders and patients/interested patient groups?

#### ***The ideal solution***

Perhaps the simplest idea would be to introduce a Europe-wide single European pack, price and name for all drugs. Though at first attractive, such a solution would quickly run into resistance on many fronts.

- i) A *single European pack* for each presentation of each medicine would eliminate the need for repackaging. However, such a policy would be difficult to introduce as countries have different preferences for a variety of reasons (economic and safety-based national regulation as well as doctors' and patients' preferences). For example, the number of tablets per pack varies: in Germany the norm is for 50-100, while in the UK it is 28. There may be also be resistance to a multi-language patient information leaflet, though most manufacturers of electrical goods use such inserts.
- ii) A *single European price* would in time almost certainly have the effect of stopping much parallel trade. Prices would be likely to rise in low-cost countries (exporters) and fall in high-cost countries (importers). But while healthcare remains fiercely protected as an exclusively national matter, and while there are so many other variables in national welfare systems, it is highly unlikely that a single price would be acceptable to governments. For example the UK is very unlikely to abolish the PPRS system which is regarded as vital to the continued success of the industry, even though profits from patented medicines may be high. Meanwhile, Greece is highly unlikely to risk higher prices which may then lead to reduced patient access to pharmaceuticals. Nevertheless, the subject emerged in the G10 medicines process, where a proposal for a single price with country-based discounts was discussed.
- iii) While *single European naming* of medicines, suggested by Sue Mitchell of Epilepsy Action, has attractions for healthcare consumers, the marketing departments of manufacturers are likely strongly to dislike the idea. New chemical entities (NCEs) are given a generic name.

At sometime during the clinical trials and before the marketing launch, the NCE is given a brand name by the manufacturer. Manufacturers cannot always use the same brand name in all EU country markets. This may be for cosmetic or phonetic reasons, or because the proposed name may be similar to another product (the same applies to most consumer goods sold in many markets—cars, food, etc.). Burstall notes that the REMIT study estimated that variations in the names of medicines had the effect of keeping out parallel imports roughly equivalent to one quarter of total imports in 1990.<sup>2</sup> Single EU naming is starting to happen more and more. One particularly well known example outside the pharmaceutical industry is the change in name in the UK from Marathon to Snickers, which was mentioned by Sue Mitchell. The switch of household cleaner Jif to Cif will also be familiar to many.

### ***Other interim solutions***

If a single name, price and packaging are not practical solutions, where should we look? The following six suggestions could be considered, though readers should note that if taken alone each of these proposals would fail to alleviate all safety concerns raised in the previous chapter.

#### ***1. Mandatory notification of intention to export***

Supply shortages have been reported in many countries including Ireland, Italy, Greece and Spain. To take preventive action on grounds of public health against possible future shortages of supply, all exporting countries could introduce *mandatory reporting* to a national regulatory authority of volumes of *all product exporting*. It has been widely reported that similar systems have been introduced in Spain and Greece, largely to prevent shortages and thereby to improve certainty in health care. Ideally, batch numbers and volumes would also be indicated, so that if recall were necessary the national authority could contact the national authority in the country of destination. In order that supplies may be increased, the national regulator could be obliged to notify manufacturers if large volumes of their products were being exported, but as far as possible they must do so without naming the exporter or revealing the destination of the exports. Failure to respect this latter caveat would place the proposal at risk of challenge as an infringement of EU law. As Kanavos and Holmes note, the response of EU institutions to these national interventions is as yet unknown.

As an extra tier of bureaucracy, such regulatory reform is certain to be resisted by parallel traders who also fear that notification of exports may lead to the limitation of supply from manufacturers. Exporters would presumably argue that manufacturers should adjust supplies to reflect their demand and that of local patients. Meanwhile, manufacturers argue that this is not possible as forecasting systems do not usually permit rapid increases in supplies for products.

Although the reporting in Spain and Greece is deemed to be confidential, the establishment of databases may lead to detailed information on the final destination of products. The response of EU institutions to these national interventions is unknown and unclear at this stage, but it is certain that the parties affected will bring them to their attention.

#### ***2. Individual patient-level continuity of medication***

Sue Mitchell of Epilepsy Action has raised important concerns regarding continuity of medication. To put these concerns in context, it should be noted that generic prescription is strongly encouraged by the UK Department of Health, but that GPs have the option to prescribe specific products, and that patients have a right to choose medication and to refuse a product at a pharmacy—although doing so may in some cases lead to delay in access to necessary treatment.

A new rule could mandate the prescription of specific products for patients presenting with certain conditions, including forms of epilepsy, and for those whose compliance may be deleteriously affected by changes in presentation (pack, name, colour, etc.) of their medication. In other words, rather than the assumption being that a patient could choose to reject an alternative, pharmacists could obtain details that would enable dispensing of the identical

product to that dispensed on prior occasions. Electronic patient records alongside the electronic transmission of prescriptions may facilitate this system.

This proposal ought to guarantee continuity of medication which should allay the concerns of certain patient groups. In terms of impact on parallel trade, it is likely to have limited direct effect on the market, since sales of certain products may experience restrictions, but those of others may conceivably increase. It would be difficult for traders to counter such a proposal from the Department of Health without appearing to be protecting their own interests to the detriment of those of patients.

Pharmacists are likely to see this idea as posing a potential threat to their income, both in terms of their margins on imported products, but also owing to the time spent checking previous prescription patterns. Meanwhile, despite the government's strong patient choice focus, the Department of Health, and in particular primary care trusts—which now control 75 per cent of the NHS budget including that for pharmaceuticals—are likely to be hostile to such a proposal owing to its long-term cost implication. The spectre of real patient choice floodgates opening is certain to be raised.

### ***3. Preventing the unpacking of medicines***

The evidence presented in Section 3 demonstrates that the unpacking of medicines is commonplace, and Kanavos and Holmes refer to a number of cases that confirm that the process is legal so long as the condition of the product is not affected. Having seen what is being done to medicines by some importers, including the cutting of blister packs, it is worth considering whether a UK market policy, on public health grounds of non-interference with original brand (including tamper-proofed) packs, would prevent some of the most worrying processes.

Such a policy would not be allowed to act as a barrier to the UK market. Thus, just as Laddie has found that repackaging is objectively necessary to gain access to the UK market,<sup>3</sup> a ban on the opening of original packs would require an over-boxing system in order to secure market access. Such a system would involve the original packs being placed inside a new box along with a PIL and appropriate new blister labelling for UK patients to stick on imported blisters.

Although this policy would enable the integrity of the product to be protected, it would not obviate the majority of errors in the repackaging process (see below). It is unlikely that such a policy would receive national political support without a significantly greater body of evidence. It is also likely that a number of manufacturers would object to an over-boxing policy on trademark protection grounds.<sup>4</sup>

This proposal might actually cut costs for some importers for some products. However in cases where the drug in the source country was packed in smaller or larger number of units per pack compared to the UK norm of 24, such a policy would act as a de facto barrier to market access. Traders and others might also argue that giving patients the responsibility for affixing blister labels gives scope for patient error and possible confusion. One solution would be to oblige dispensing pharmacists to unpack and 'reconstruct' the pack for patients—a potentially time consuming activity.

With these various concerns in mind, it is worth considering what would spur the Department of Health to attempt to ban the opening of tamper-proofed products? The answer lies in a significant larger body of evidence of public health concerns related to repackaging.

A policy of over-boxing may help prevent subsequent repackaging acting as a conduit for counterfeit products.

### ***4. Improving repackaging***

Repackaging is permitted so long as the condition of the product is not affected and is usually objectively necessary to market in the UK. But in light of the repackaging errors<sup>5</sup> and disturbing practices seen (e.g. cutting of blister packs, missing information regarding side effects, warnings and safety restrictions not shown, all of which could pose a danger to health) there could be a case on grounds of public health for stricter regulation and inspection of repackaging processes

and good distribution practices (GDP) throughout supply-chain. GDP is the part of quality assurance which ensures that products are consistently stored, transported and handled under suitable condition as required by the marketing authorisation or product specification.<sup>6</sup>

Specifically, there could be an obligation to submit genuine examples of the product to be marketed, not just packaging, labelling and PIL when applying for marketing authorisation.

Any changes to repackaging process regulation are likely to be seen as unnecessary and bureaucratic attempts to limit trade. Importers are likely to be supported by the MHRA in their suggestion that GDP is already adequately implemented and inspected.<sup>7</sup> According to the MHRA, inspections are carried out whenever a company has applied for a wholesale dealer's licence and periodically during the course of a licence. The maximum interval is four years for wholesalers.<sup>8</sup>

Whether or not four years is often enough, in the course of research for this report a number of stakeholders expressed concerns that the existing UK regulatory authority, the MHRA is unable to dedicate sufficient time to the authorisation processes and inspection. An increase in administrative workload would require an increase in resources of regulatory and inspection bodies across Europe. Such a financial commitment would be difficult to sell politically at a time when the Department of Health's arms-length bodies are being radically culled.

Tighter regulation of repackaging alone is not likely to impact on the likelihood of counterfeits entering the supply chain. It is the very existence of repackaging that concerns the manufacturers.

## **5. Measures to secure supply chain and improve product recall**

### **5.1 EU-wide batch number notification scheme**

According to EFPIA, traceability problems caused by irregular and unpredictable parallel trade flows may also have important implications, particularly when an urgent recall of products is needed in light of a significant risk to public health. GMP and GDP demand that batch traceability is always possible from manufacturer to wholesaler, but manufacturers and their associations argue that it is not always possible beyond the wholesaler, particularly to the level of short-line wholesalers and pharmacies. Furthermore, in the Netherlands batch numeration is according to a regulation which takes into account the date of manufacturing. In the case of parallel trade, a batch number is allotted by taking into account the date of the repackaging, potentially compromising the traceability and the possibility of batch recall.<sup>9</sup>

Perhaps batch number recording in the European supply chain ought to be centralised and standardised. Such a system would require manufacturers to submit electronically to a central authority's (perhaps EMEA) database details, including batch number and expiry date, of all their products. Any wholesaler or importer (and hospital or pharmacy) subsequently purchasing the product would be obliged to submit details of batch numbers and destinations to the central database. The database would confirm the authenticity of the product. Every batch number would establish a firm provenance that would facilitate product recall.

Traders and MHRA will argue that recalls are not problematic and that GDP requires that distributors maintain records to enable effective recall.<sup>10</sup> Such a scheme might be regarded as an extra tier of bureaucracy that would act as a minor barrier to trade. Firm assurances would have to be made that manufacturers would not have access to the database and thus would not be assisted in the restriction of parallel traders' access to their products.

In practical political terms it may be impossible for governments and regulatory authorities in Europe to reach agreement on such a system, particularly regarding ownership of and access to data.

### **5.2 Notification of batch numbers of all products exported within EU and UK**

If we assume that manufacturer's supply chain loss of control, integrity and also counterfeit threat concerns are genuine, the following three proposals might be considered.

The first proposal, a variation on 5.1, would involve the electronic notification to and storage of all exported batch numbers and expiry dates by the UK national authority. Manufacturers

would have no direct access to this database. But it might be difficult for national authorities to check the batch numbers of products with manufacturers without drawing attention to the identity of the importer, thus risking continuity of supply in the country of origin and thereby restricting parallel trade. Therefore an arms-length system would be necessary which involved a centralised EU database.

Wholesalers would submit to the EU-level database the source and destination of products concerned. This information would be available to national regulatory authorities.

If an application for an import licence were granted, the national authority in the UK, the MHRA, could cross-check with manufacturer X via the EU database to ascertain if imports were genuinely made by manufacturer X. If there was no problem with the medicine the manufacturer would remain unaware of its destination. The only need to notify a manufacturer of an imported product's location would be in the case of a drug alert concerning their products. If a product recall were necessary it would be easier to identify where products were in the supply chain.

Although this system would improve supply chain certainty, it would be expensive to set up and might not significantly improve current recall systems.

### 5.3. 2-D bar-coding<sup>11</sup>

In combination with 5.1 or 5.2, 2-D bar-coding should enable the tracking of medicines, and improve the safety of their provision throughout the European supply chain, from manufacturer to patient. The NHS is gearing-up for use of this technology.

In his January 2004 report on improving medication safety for NHS patients, Britain's chief pharmacist said that: 'greater use of electronic prescribing in hospitals, bar-coding technology and robotic dispensing have the potential to reduce the risk of medication errors'.<sup>12</sup>

As electronic prescribing and electronic patient records are introduced over coming years, products that are not bar-coded will not be able to enter hospitals and pharmacies. Roughly 70 per cent of medicine packages in the UK already have a bar-code. However, some symbologies are global, while others are bespoke.<sup>13</sup> Until recently there has been no UK national—let alone European—medicines coding system. This is changing as part of the NHS' National Programme for Information Technology.<sup>14</sup> Actual Medicinal Product Pack (AMPP) are one of the concept classes found in the NHS's new electronic dictionary of medicines. AMPPs are unique for a product, thus this unique AMPP can be given a bar code.<sup>15</sup>

Of course, this NHS bar-coding programme does not offer a Europe-wide solution. Thus parallel traders, like manufacturers, would have to repackage and carefully add the appropriate bar code. A European standard system would be preferable.

*Expiry dates and batch numbers:* Unfortunately, standard EAN-13 bar-coding<sup>16</sup> is not able to hold batch numbers or product expiry dates. The solution thus lies in 2-D bar codes, whereby the familiar existing code would have another layer on top containing vital batch number and expiry date information.

Furthermore, as more technologically advanced solutions are on the horizon, the government should consider the introduction of a system that will be subsequently adaptable.

In the meantime, 2-D bar-coding offers many advantages. For example, expiry dates could be better monitored, and product recall would be better enabled. Medication dispensing errors (dose, etc.) should be limited, and automatic restocking systems could be established. However, it is likely that many manufacturers and parallel importers would have to change their packaging processes in order for batch numbers and expiry dates to match those of the product. This is likely to involve some short-term cost and might meet resistance.

### 5.4 Radio frequency identification

RFID is an even more advanced and flexible long-term solution to supply chain security. It would enable the tracking of medicines by pack, rather than by batch. In combination with batch notification schemes 5.1 or 5.2, it should permit the tracking of medicines throughout the European supply chain, from manufacturer to patient. According to the e-centre:

like a bar code or an electronic data interchange (EDI) network, an [RFID device] is a data carrier. A bar code carries data in a visible symbol and is read at optical or infrared wavelengths; an RFID device (or tag) carries data programmed into a chip and operates at a wide range of radio frequencies. Essentially all tags comprise a semiconductor chip with memory, processing capability and a transmitter connected to an antenna (aerial).<sup>17</sup>

This method of tracking would see every pack of medicines produced have its own unique number, a number that could be entered on a central database when imported. The technology is likely to be available in a few years' time and is already regarded as a major tool in the fight against global counterfeiting. The advantage of RFID over bar-coding is one of detail. While bar-codes could enable the tracking and recall of products by batch number, RFID technology would be able to track every single package from manufacturer down to pharmacist and patient. Smart tags could also tell if cold-store products had been stored correctly.

Some, including leaders of cash-strapped healthcare systems, may ask whether RFID is necessary in Europe, since there is little evidence of counterfeit medicines entering the supply chain.

Such technology would certainly add to the cost of medicines and so may be resisted by some actors, including patients and health insurance organisations. Moreover, some concerns about privacy and access to data are likely to be raised by parallel traders and manufacturers, not to mention citizens and governments.

### ***6. EU enlargement and the derogation principle***

In Part I, Kanavos and Holmes reminded us that the EU has just admitted new member states, eight from former Eastern Europe plus Cyprus and Malta. There is a fear on the part of manufacturers that parallel importers may seek the services of lower cost pharmaceutical repackaging in the new member states. Such activities may weaken the supply chain, amounting to a patient-safety loop-hole.

Parallel trade from the newly admitted member states will be subject to the application of the principle of derogation, which applies to the eight Eastern European members, but does not apply in Cyprus and Malta. As intellectual property rights for individual products are weaker in the eight accession countries compared with the EU-15, no parallel trade is allowed from any of those eight member states to EU-15. But parallel trade within the territory comprising the ten new member states is permitted. The EU-15 have signed up to a document outlining the new rules and accepting the principle of derogation, but Kanavos and Holmes suggest there are few signs concerning the potential for enforcing this. Therefore this may pose a threat of exportation from one of the eight newly acceding Eastern European countries to the old EU-15, including the UK, if sufficient price differences exist.

It is important that the rules relating to parallel importing from EU-8 to EU-15 are clarified and strongly enforced by European and national regulators.

The following table sets out in brief the practical possible solutions to the various safety issues that have been raised in the course of our project. None of these is exhaustive, rather they are designed as a spur for future discussion. Again, readers will appreciate that if taken alone each of these proposals would fail to alleviate all safety concerns.

**Table 3**  
*Summary of Potential Parallel Trade Policy Proposals*

Potential Safety Issue	Civitas Proposal	Effect on Parallel Trade/ Response of traders	Effect on Threat from Counterfeits
<b>Current unquestionable threat to patient safety/public health</b>			
1. Supply shortages in source country  Reported in a number of countries—e.g. Ireland, Italy, Greece, Spain	<i>Legal Context:</i> Articles 28 and 30 EC. Spanish do this already on grounds of public health; access to necessary medicines. Also see Bayer judgment 2004  <i>Grounds for proposal:</i> public health  In all countries of origin (Spain, Greece, France, etc.), introduce <b>mandatory reporting</b> to a national regulatory authority of <b>the destination of products exported</b> . Batch numbers and volumes should be indicated. The national regulator could be obliged to notify manufacturers if large volumes of their products were being exported, but as far as possible must do so without naming the exporter	An extra tier of bureaucracy—likely to be resisted by parallel traders. Traders would fear that notification of exports would lead to the cutting of supply from manufacturers  Would argue that manufacturers should adjust supplies to reflect their demand and that of local patients	Unlikely to have any effect
2. Individual patient-level continuity of medication in importing country	<i>Legal Context:</i> generic prescription is strongly encouraged by DoH. GPs have the option to prescribe specific products. Patients have a right to choose medication  <i>Grounds for proposal:</i> public health  A new rule could <b>mandate the prescription of specific products for patients presenting with certain conditions</b> including forms of epilepsy and for those whose compliance may be deleteriously affected by changes in presentation of their medication	No direct effect  May limit sales of certain products but increase those of others	None
<b>Potential threats to patient safety/public health</b>			
3. Unpacking of medicines	<i>Legal Context:</i> ECJ various, permitted so long as the condition of the product is not affected. Articles 28 and 30  <i>Grounds for proposal:</i> public health  A UK market policy of non-interference with original brand (including tamper-proofed) packs would require <b>an over-boxing system</b> in order to secure market access. Original packs would be placed inside a new box along with a PIL and appropriate new blister labelling for UK patients/dispensing pharmacists to stick on imported blisters  NB: This policy would enable the integrity of the product to be protected but would not obviate the majority of errors in the repackaging process (see No. 4)	This proposal might cut costs for some importers for some products  However in cases where the drug in the source country was packed in smaller or larger number of units per pack compared to the UK norm, such a policy would act as a barrier to market access  Traders and others might also argue that giving patients/pharmacists the responsibility for affixing blister labels gives scope for patient/pharmacist error and possible confusion  May also meet resistance from pharmacists	May help prevent subsequent repackaging acting as a conduit for counterfeit products

Table 3 cont'd over/

<p>4. Repackaging errors</p>	<p><i>Legal Context:</i> Articles 28 and 30, significant volume ECJ case law; repackaging is permitted so long as the condition of the product is not affected. It is usually objectively necessary to market in the UK <i>Grounds for proposal:</i> public health</p> <p><b>Stricter regulation throughout supply-chain.</b> Examples of the product to be marketed, not just packaging could be submitted when applying for marketing authorisation. GDP to be enforced throughout supply chain</p>	<p>Likely to be seen as unnecessary bureaucracy GMP already adequate</p>	<p>Tighter regulation of repackaging alone is not likely to impact on the likelihood of counterfeits entering the supply chain</p>
<p>5. Need to secure supply chain and improve product recall</p> <p>There is a good case to be made for better tracking of where medicines are in the supply chain. Systems for recalls impacting on more than one country must be effective.</p>	<p><i>Legal Context:</i> Article 30. GMP, GDP <i>Grounds for proposal:</i> public health</p> <p><b>5.1 EU-wide batch number notification scheme</b> This system would require manufacturers to submit electronically to a central authority (perhaps EMEA) database details, including batch number and expiry date, of all their products. Any wholesaler or importer (+ hospital + pharmacy) subsequently purchasing the product would be obliged to submit details of batch numbers and destinations to the central database. The database would confirm the authenticity of the product</p> <p><b>5.2 Notification of batch numbers of all products imported to EU UK</b> This proposal would involve the electronic notification to and storage of all imported batch numbers and expiry dates by an EU and national authority (MHRA). National authority could x-ref with manufacturer to ascertain if imports were genuine</p> <p><b>5.3. EU-wide 2D Bar-coding of medicines</b> This system might complement 5.1 and 5.2 and would add to the government's current NHS medicines bar-coding programme which is designed to improve safety of the provision of medicines. In combination with 5.1 or 5.2, 2-D bar-coding should enable the tracking of medicines throughout the European supply chain, from manufacturer to patient</p> <p><b>5.4 Radio Frequency Identification</b> RFID would enable the tracking of medicines by pack/blister, rather than by batch. In combination with 5.1 or 5.2, it should enable the tracking of medicines throughout the European supply chain, from manufacturer to patient</p> <p>Some concerns about privacy and access to data are likely to be raised</p>	<p>Might be regarded as an extra tier of bureaucracy that would act as a minor barrier to trade</p> <p>Firm assurances would have to be made that manufacturers would not have access to the database</p> <p>Manufacturers would have no direct access to this database. But it might be difficult for national authorities to check the batch numbers of products with manufacturers, without drawing attention to the identity of the importer, thus restricting parallel trade</p> <p>This system would involve additional costs for importers</p> <p>RFID may be resisted on cost grounds. The likely effect on parallel trade depends on who has access to and who controls the data collected</p>	<p>5.1 Ought to help prevent c-f products being dispensed to patients</p> <p>5.2 Ought to help ascertain authenticity of medicines.</p> <p>5.3 Ought to act as a deterrent</p> <p>5.4 Even more likely to act as a deterrent</p> <p>There is also a concern that without adequate safeguards, product identities may be stolen</p>
<p>6. EU Enlargement</p>	<p><i>Legal Context:</i> derogation from importing rules. Less patent protection in 8 of the 10 new member states (not Cyprus and Malta) <i>Grounds for proposal:</i> public health</p> <p>The rules relating to parallel importing from EU-8 to EU-15 must be clarified and enforced</p>	<p>Importers may seek the services of lower-cost repackaging in certain new members states. Anything that restricts such activity may be regarded as a barrier to trade by those new members and also the companies involved</p>	<p>Potential weak link in supply chain</p>

*Source:* Based on author's research including interviews and correspondence with manufacturers, wholesalers, parallel traders, the MHRA, Department of Health, and national and EU-level trade associations.

## Conclusion

### Benedict Irvine

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#### ***Is parallel trade policy development by consensus a pipe dream?***

As an organisation, Civitas is rightly labelled ‘free-market-orientated’. We approach parallel trade with the view that there is nothing wrong with it *per se* within a free trade area. However, varying national government regulation of pricing and access to markets within that free trade area give rise to legitimate complaint by the pharmaceutical industry.

Panos Kanavos and Paul Holmes have produced a valuable independent report into the EU-UK parallel trade market. This is likely to become a key reference for all those interested in parallel trade. The hypothesis of Part II of this paper was that parallel trade may undermine patient safety. Kanovos and Holmes also touch on this subject. Although some serious problems have emerged, the hypothesis is not, as yet, satisfactorily proven. Civitas has carried out both semi-structured interviews and less formal conversations with a range of stakeholders<sup>1</sup> in the course of this project, particularly with view to eliciting stakeholder response to a few regulatory reform proposals. Responses were passionately voiced from all quarters. Indeed, one of the difficulties encountered in the project was the exaggerated nature of much of the debate. The measured responses tended to be from those unwilling to answer questions. As such, it is hard to envisage a consensus for reform as there is so little agreement as to what problems there are, let alone what solutions may work. Off-the-record discussion reveals significantly greater consensus, but with such strong vested interests to protect, those views are unlikely to be expressed publicly for the foreseeable future.

Should our focus be on patient safety or on trademark issues? The European pharmaceutical market is complex, and beyond the nationally-based segmentation of the European pharmaceutical market, there are real splits within the research industry in their approach to parallel-trade regulation. Post-enlargement, there is a little more consensus regarding the threat of counterfeiting in Europe, but the leading research companies rarely, if ever, communicate with each other on the subject. They presumably fear the accusation of collusion and subsequent legal action on the basis of a breach of EU competition law.<sup>2</sup> Perhaps the research-based sector could make the first move and undertake to pay for a beefed-up MHRA and EMEA (there is precedent for this in the US<sup>3</sup>). Doing so would signal not only that patient safety concerns were legitimate, but that the general public’s faith in the quality and efficacy of medicines is paramount to the industry. However, such a move would require concerted action on the part of the industry and they are reluctant to act *en masse*.

Importers believe that to imply that parallel trade is a leaky, unsafe channel is an unjustifiable smear. There are structural divisions among parallel traders too; full-line traders are likely to have a markedly different perspective from short-line traders. The former provide a genuine public service and have great responsibilities towards patients. The latter pursue legitimate opportunities, but don’t appear to have the same quasi-integrated relationship with national health services. Additionally, as in any business, new thrusting entrants want to generate and improve their reputation and market share, while established highly professional firms seek to protect their market and may rest on their metaphorical laurels. Furthermore, any sector of the economy is likely to have its rogues. So we must ask whether this diverse range of interests can be reconciled. Should regulation focus on the rogues or those players whose practices are flawless?

The UK Government has to consider the existing evidence on the economic and welfare costs of parallel trade (see Kanavos and Holmes), while at the same time remaining sensitive to the fact

that its PPRS system, which could be said to drive parallel trade, is an essential force of the UK's research-based pharmaceutical industry, which in turn is a major employer.

Potential allies in the patient organisation world have very important patient safety concerns that should be acted upon. However, those involved directly with this project are open to the criticism that their particular concerns are not directly related to parallel trade. As such, they do not offer a united front either. Although parallel trade is certainly a genuine concern of theirs, Depression Alliance appears mainly concerned about unregulated access to medicines through mail order exacerbated by online pharmacies. Counterfeit products are a threat in this context, but perhaps the more worrying issues are self-diagnosis and lack of doctor contact. Meanwhile, a dispassionate assessment of Epilepsy Action's position might conclude that it is primarily concerned with continuity of medication, which is indirectly affected by parallel trade.

Our philosophical approach to the supply of medicine supply is akin to the research industry's: we aim for the smallest possible role for government that is consistent with access to quality medicines. There must be a legitimate role for governments in providing the framework for healthcare systems and this framework includes regulatory régimes. Patient safety and the threat of counterfeiting may concern many, but the simple regulatory solutions outlined above might obviate those concerns. If this report serves to enable or promote some rational cool-headed debate, it will be of service to the public.

**Appendix 1**  
***Questionnaire addressed to MHRA on regulatory issues surrounding parallel importation of pharmaceuticals***

MHRA (Pharmaceutical enquiries, Parallel Imports, Drug/Device Unit, MHRA)

- 1) What are the regulatory procedures regarding the approval of parallel-imported medicines and how do these compare with locally-sourced products?
- 2) Given that their drug regulatory agencies do not have oversight over foreign supplies, how do countries address issues of:
  - a) Safety?
  - b) Inadequate labelling?
  - c) Counterfeiting?
- 3) To what extent have countries, as a result of drugs received through parallel importation, had:
  - a) Expired drugs?
  - b) Labelling and packaging problems?
  - c) Unsafe handling?
- 4) What technology exists to minimise the effect of counterfeit and/or expired drugs, labelling problems or unsafe handling?
- 5) Is there a problem with unapproved drugs crossing the border?

## Notes

### Foreword

- 1 West P., Mahon, J., *Benefits to Payers and Patients from Parallel Trade*, York Health Economics Consortium, University of York, May 2003.
- 2 Kanavos, P., *et al.*, *The Economic Impact of Pharmaceutical Parallel Trade in European Union Member States: A Stakeholder Analysis*, 2004.
- 3 EAEPC, 'LSE Study on Parallel Trade Seriously Flawed, Results Invalid, says EAEPC, Press Release, 25 March 2004.
- 4 *Pharmaceutisch Weekblad*, 1 October 2004, Jaargang 139 Nr. 40, pp. 1300-02.

### Part I

#### Executive Summary

- 1 Regional exhaustion (within the context of the European Union, 'region' defined as the member states of the EU) refers to a situation where once a product has been legitimately put on the market in one member state, it is a breach of the principle of the free movement of goods (Article 28 of the EU Treaty) to prevent the product to be resold in another member state even if the product is protected by the exclusivity granted by a patent or other intellectual property right in the latter state.
- 2 The concept of dual pricing refers to a practice whereby for the same product manufactured in one country, the manufacturer will charge one price for the market in question and a different price in other markets if the product in question is exported to these markets with or without the manufacturer's authorisation. In the case at hand, the legality of charging one price in one member state and an 'export' price in other member states, when a product is exported, has been challenged.
- 3 Using anti-competitive practices to exploit its monopoly power in the market.

#### 1: Introduction

- 1 Abbott, F.M., First Report (Final) to the Committee on International Trade Law of the International Law Association on the Subject of Parallel Importation, *Journal of International Economic Law* 1998;1:607-636.
- 2 Ahmadi, R. and Yang, B.R., 'Parallel imports: challenges from unauthorised distribution channels', *Marketing Science*, 2000;19(3):279-294; Ganslandt, M., Maskus, K.E., *Parallel imports of pharmaceutical products in the European Union*, The Research Institute of Industrial Economics, Working Paper No 546; 2001.
- 3 Philipson, A., *Guide to the Concept and Practical Application of Articles 28-30 EC*, Commission of the European Communities, DG Enterprise, Brussels, January 2001.  
 Joint Cases C-427/93, C-429/93, C-436/93 Bristol-Myers Squibb v. Paranova [1997] ESR 102.  
 European Court of Justice, ECJ Case C-443/99 Merck, Sharp & Dohme GmbH v. Paranova Pharmazetika Handels GmbH, 1999.  
 European Court of Justice, ECJ Case C-143/00 Boehringer Ingelheim GmbH, Glaxo Group Ltd and others v. Dowelhurst Ltd and Swingward Ltd, 2000.  
 European Court of Justice, ECJ Cases C-267/95 and C-268/95 Merck and Others v. Primecrown and Others and Beecham Group v Europharm of Worthing, Judgment of 5th December 1996.  
 European Court of Justice, ECJ Case T-41/96 Bayer AG v. Commission of the European Communities, Judgement of 26 October 2000.  
 European Court of Justice, ECJ Case C-433/00 Aventis Pharma Deutschland GmbH v. Kohlpharma GmbH and MTK Pharma Vertrieb-GmbH, Comment of 19 September 2002.  
 European Court of Justice, Judgment of the Court of Justice in Joined Cases C-2/01 P and C-3/01 P: *Bundesverband der Arzneimittel-Importeure and Commission of the European Communities v Bayer AG*; Press Release No. 01/04,  
<http://curia.eu.int/jurisp/cgi-bin/form.pl?lang=en&Submit=Submit&docrequire=alldocs&numaff=C-2%2F01+P&datefs=&datefe=&nomusuel=&domaine=&mots=&resmax=100>; 6 January 2004, accessed 9 January 2004.  
 European Court of Justice, Common Origin not prerequisite for parallel trade, Opinion, ECJ case C-112/02, Kohlpharma GmbH vs. Federal Republic of Germany, 12 September 2003.
- 4 Barfield, C.E. and Groombdidge, M.A., 1998.
- 5 Abbott, First Report (Final) to the Committee on International Trade Law of the International Law Association on the Subject of Parallel Importation, 1998.
- 6 Knox, D. and Richardson, M., 'Trade policy and parallel imports', *European Journal of Political Economy* March 2003;19(1):133-151.

- 7 Borodoy, C. and Jelovac, I., 'Pricing and welfare implications of parallel imports in the pharmaceutical industry', MERIT, Maastricht Economic Research, Institute on Innovation and Technology Working Paper 4, the Netherlands, 2003.
- 8 Mauleg, D. and Schwartz, M., 1998.
- 9 Hausman, J.A. and MacKie-Mason, J.K., 'Price discrimination and patent policy', *RAND Journal of Economics*, 1988;19: 253-265.
- 10 Mauleg, D. and Schwartz, M., 1994, p. 169.
- 11 Maskus, K.E., 'Parallel imports in a model of vertical distribution: theory, evidence and policy', *Pacific Economic Review*, 2002;7:319-334.  
Knox, D. and Richardson, M., 'Trade policy and parallel imports', *European Journal of Political Economy*, 2002;19:133-151.  
Richardson, M., 'An elementary proposition concerning parallel imports', *Journal of International Economics*, 2002;56:233-245.  
Maskus, K.E., and Chen, Y., 'Vertical price control and parallel imports: theory and evidence', *Review of International Economics*, 2003.  
Ahmadi, R. and Yang, B.R., 'Parallel imports: challenges from unauthorized distribution channels', *Marketing Science*, 2000;19(3):279-294.  
Mauleg, D.A. and Schwarz, M., 'Parallel Imports, demand dispersion and International Price Discrimination', *Journal of International Economics*, 1994;37:187-196.
- 12 Danzon, P., 'The Economics of parallel trade', *Pharmacoeconomics*, 1998.

## 2: Legislative Background

- 1 Commission of the European Communities, 'Commission Communication on parallel imports of proprietary medicinal products for which marketing authorisations have already been agreed', Communication from the Commission, Brussels, 30 December 2003, COM(2003)839 final.
- 2 Case 104/75 Adrian DePeijper, Managing Director of Centrafarm BV [1976] ECR 613.
- 3 Case 120/78 Cassis de Dijon [1979] ECR 649.
- 4 Characterised as an agreement between undertakings prohibiting a trader from exporting from one member state to another by a dominant firm thereby affecting free trade.
- 5 Despite economists advocating Ramsey pricing—recovering more of the overhead (R&D) costs from those more able to pay than from others, provided that the variable costs of every sale are recovered.
- 6 Case T-41/96 Bayer AG v. Commission of the European Communities, Judgement of 26 October 2000.
- 7 European Association of Euro-Pharmaceutical Companies Website. <http://www.eaepc.org/parallel.htm>. Accessed 20 June 2003.
- 8 Excipients are inert substances used as a medium in pills and capsules that form a vehicle for delivery of a drug or dietary supplement. For more information go to: <http://www.ipep.org/publicdomain.htm>

## 3: Regulatory Issues

- 1 Editor's note: A case of counterfeiting was reported on 24 August 2004; counterfeit Cialis 20 mg Tablets was discovered, giving rise to an MHRA product recall of two batch numbers which were not licensed in the UK. Lilly ICOS UK Ltd is assisting in the recall. Cialis manufactured and distributed by Lilly ICOS are not affected. Initial analytical tests of counterfeit material do not indicate that this material poses an immediate risk to patients. An inquiry has been set up to establish how this counterfeit Cialis entered the UK legitimate supply chain. At this stage there is no definitive evidence that the counterfeit product entered the UK legitimate supply chain through parallel trade. For further detail go to the following weblinks: [http://medicines.mhra.gov.uk/ourwork/monitorsafequalmed/defmedsrepcen/counterfeitcialis\\_230804.pdf](http://medicines.mhra.gov.uk/ourwork/monitorsafequalmed/defmedsrepcen/counterfeitcialis_230804.pdf)  
[http://www.abpi.org.uk/press/press\\_releases\\_04/040824.asp](http://www.abpi.org.uk/press/press_releases_04/040824.asp)

## 4: Institutional Policies Encouraging the use of PI Medicines

- 1 Assuming that patients' perception of a locally-sourced and a PI pharmaceutical is exactly the same.
- 2 West, P. and Mahon, J., *Benefits to Payers and Patients from Parallel Trade*, York: York Health Economics Consortium, May 2003, <http://www.yhec.co.uk>.
- 3 Macarthur, D., Submission to G-10 Medicines, 2002.

- 4 West and Mahon, *Benefits to Payers and Patients from Parallel Trade*, 2003.

#### 5: UK Structures

- 1 According to BAEPD, applicant companies must be registered in England; must hold a Wholesale Dealers Licence issued by the MCA [MHRA]; must hold a Manufacturer's (Assembly Only) Licence issued by the same regulatory body; and must hold a minimum of 100 Parallel Import Product Licences (PIPLs) (source: <http://www.baepd.co.uk/>).
- 2 Necessity Supplies Ltd. Notes to the Financial Statements for the year ended 31 May 2003.

#### 6: The Economic Impact of Parallel Trade

- 1 While analysing in detail all the methodological issues raised by the three studies is outside the scope of this book, the studies are in the public domain and readers are encouraged to study them.
- 2 ESRC; Intellectual Property Rights and Parallel Trading in Pharmaceuticals.
- 3 ESRC; Intellectual Property Rights and Parallel Trading in Pharmaceuticals.
- 4 Kanavos, P., 'The Economic Impact of Pharmaceutical Parallel Trade in European Union Member States: A Stakeholder Analysis', London School of Economics, 2004.
- 5 West, P., *Benefits to Payers and Patients From Parallel Trade*, York Health Economics Consortium; May 2003.
- 6 West, *Benefits to Payers and Patients From Parallel Trade*, 2003.
- 7 Kanavos, P., Costa-I-Font, J., Merkur, S. and Gemmill, M., 'The economic impact of parallel trade: a stakeholder analysis', *LSE Health and Social Care Special Research Paper*, January 2004.
- 8 Kanavos, P., *Pharmaceutical Pricing and Reimbursement in Europe, 2002*, Surrey: PJB Publications Ltd, May 2002.
- 9 Morais, R.C., 'Psst... Wanna Buy Some Augmentin?', *Forbes* 2000, 12 April 2004.
- 10 West, *Benefits to Payers and Patients From Parallel Trade*, 2003.

## Part II

### 2: Stakeholder Views

- 1 This clarification explains why there is no published reference that cites this figure.
- 2 Satchwell, G., *A Sick Business. Counterfeit Medicines and Organised Crime*, London: The Stockholm Network, 2004.
- 3 Harper, J., Draft report on counterfeiting medicines presented to the CoE ad hoc Committee on Counterfeit Medicines, December 2004.
- 4 Szymanski, S., *Intellectual Property Rights and Parallel Trading in Pharmaceuticals*, London: Imperial College, 2004.

### 3: Evidence of Patient Safety Concerns

- 1 Personal communication.
- 2 Personal communication.
- 3 A case of counterfeiting was reported on 24 August 2004; counterfeit Cialis 20 mg Tablets were discovered, giving rise to an MHRA product recall of two batch numbers which were not licensed in the UK. Lilly ICOS UK Ltd is assisting in the recall. Cialis manufactured and distributed by Lilly ICOS are not affected. Initial analytical tests of counterfeit material do not indicate that this material poses an immediate risk to patients. An inquiry has been set up to establish how this counterfeit Cialis entered the UK legitimate supply chain. At this stage there is no definitive evidence that the counterfeit product entered the UK legitimate supply chain through parallel trade. For further detail go to the following weblinks:  
[http://medicines.mhra.gov.uk/ourwork/monitorsafeequalmed/defmedsrepcen/counterfeitcialis\\_230804.pdf](http://medicines.mhra.gov.uk/ourwork/monitorsafeequalmed/defmedsrepcen/counterfeitcialis_230804.pdf)  
[http://www.abpi.org.uk/press/press\\_releases\\_04/040824.asp](http://www.abpi.org.uk/press/press_releases_04/040824.asp)
- 4 [http://www.abpi.org.uk/press/press\\_releases\\_04/040824.asp](http://www.abpi.org.uk/press/press_releases_04/040824.asp)
- 5 Maclean, N. (ed.), *Parallel Trade in Medicines*, London: Social Market Foundation, 2004.
- 6 Maclean, N. (ed.), *Parallel Trade in Medicines*, London: Social Market Foundation, 2004.
- 7 According to an MHRA representative, a review of statistics held for the year 01-Apr-2003 to 31-Mar-2004 reveals the following. Two situations affecting parallel-imported products apply:
  - a) Where the issue affects the PLPI holder only; in the year 01-Apr-2003 to 31-Mar-2004, for example, this

accounted for approximately 14.5 per cent of all recalls. These were in fact all company-led recalls not involving an MHRA issued Drug Alert.

b) Where the issue affects the original branded product and therefore all PLPI licence holders; in the year 01-Apr-2003 to 31-Mar-2004, for example, one Drug Alert (approx. seven per cent) also involved parallel imported product.

- 8 Personal email communication with MHRA representative.
- 9 Personal email communication with MHRA representative.
- 10 MacArthur, D., 'Parallel trade in medicines across the EU should be supported', Consumers' Association, *Consumer Policy Review*, 19 February 2001.

#### 4: Proposals for Reform

- 1 Article 28: Quantitative restrictions on imports and all measures having equivalent effect shall be prohibited between member states  
Article 29: Quantitative restrictions on exports and all measures having equivalent effect shall be prohibited between member states  
Article 30: The provisions of Articles 28 and 29 shall not preclude prohibitions or restrictions on imports, exports or goods in transit justified on grounds of public morality, public policy or public security; the protection of health and life of humans, animals or plants... Such prohibitions or restrictions shall not, however, constitute a means or arbitrary discrimination or a disguised restriction on trade between member states. Consolidated version of the Treaty Establishing the European Community. 2002.  
[http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/c\\_325/c\\_32520021224en00010184.pdf](http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/c_325/c_32520021224en00010184.pdf)
- 2 Burstall, M.L. and Senior, I.S.T., *Undermining Innovation: parallel trade in prescription medicines*, London: IEA Health and Welfare Unit, 1992, p. 39, citing *Scrip*, 13 October 1989, 1455, 4; see also *ibid.*, 5 June 1991, 1662, 4. REMIT Consultants for Directorate-General 4 of the European Community: Impediments to parallel trade in pharmaceuticals within the European Community, 1992, European Commission; *Scrip*, 5 June 1991, 1622, 4.
- 3 See this summary from Ashurst Morris Crisp: <http://www.ashursts.com/pubs/pdf/2478.pdf>
- 4 ECJ, various.
- 5 Readers will recall that Kanavos and Holmes suggest that the rate at which errors occur is falling.
- 6 Source: <http://medicines.mhra.gov.uk/ourwork/ensurequalmed/gmpandgdp.htm>
- 7 Source: communication with EAEPC and MHRA.
- 8 Source: <http://medicines.mhra.gov.uk/ourwork/ensurequalmed/gmpandgdp.htm>
- 9 Source: communication with manufacturers and EFPIA; Kanavos and Holmes, Part I.
- 10 Source: communication with EAEPC and MHRA.
- 11 'Bar code symbolologies. A bar code represents data in a machine readable form, which means they are used to replace manual key entry. A bar code is a pattern of bars and spaces holding a unique identification number. The bar code can then be decoded or read by a scanner to retrieve the information from a database. The information encoded in the bar code is shown in human readable format beneath the bar code. Automatically capturing data through bar codes is increasingly used to speed data collection and minimise errors caused by manually keying in data.' 'The EAN/UPC bar codes are a family of four linear bar codes encoding the 8, 12 and 13-digit GTINS. These bar codes can be read omni-directionally (in any direction) and are therefore suited for fast scanning and manual handling environments. The EAN-13 and UPC-A bar codes are the most widely used because they can be used at any point within the supply chain. The EAN/UPC bar codes are the only symbols accepted at the retail point of sale.' [http://www.e-centre.org.uk/free\\_txt\\_temp.asp?fid=87](http://www.e-centre.org.uk/free_txt_temp.asp?fid=87)
- 12 Tracey Logan, London's Charing Cross hospital is beginning trials this month of a system using bar codes on patients. <http://news.bbc.co.uk/2/hi/technology/3776475.stm>
- 13 [http://www.e-centre.org.uk/free\\_txt\\_temp.asp?fid=87](http://www.e-centre.org.uk/free_txt_temp.asp?fid=87)
- 14 NHS bar codes are at an early stage of development, but are already being piloted in two hospitals. Hospital authorities hope the system will improve patient safety by reducing drug-related errors on the ward. Charing Cross is one of just two hospitals in the world testing the new bar coding system, which links patients to a computerised drugs trolley, or Smart Cart, on the ward.. Tracey Logan, London's Charing Cross hospital is beginning trials this month of a system using bar codes on patients.  
<http://news.bbc.co.uk/2/hi/technology/3776475.stm>
- 15 Key information from e-commerce expert at PASA.
- 16 <http://www.e-centre.org.uk/>

17 <http://www.e-centre.org.uk/>

#### **5: Conclusion**

- 1 Including academics, industry consultants, importers the brand industry, industry associations, the UK Department of Health, and regulators.
- 2 Articles; 81 and 82 EC Treaty.
- 3 Source: conversation with EU and US industry expert. Some parallels could also be drawn with the recent decision of Philip Morris to assist in the fight against counterfeit cigarettes.