Parallel trade in the EU and US pharmaceutical markets

Amanda Wearing, Ian Kirby, Marleen Van Kerckhove and William Vodra, Arnold & Porter LLP

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There is a high level of parallel trade in the EU, where there is no harmonisation in product pricing and significant commercial opportunities for distributors to buy in a low price country, ship the product to a higher price market and undercut the local price. Perhaps because of the many years of experience of parallel trade in the EU, this activity is reasonably well regulated by a combination of regulatory controls and the rules relating to the protection of intellectual property rights.

In contrast, parallel trade is a relatively new concept in the US. Historically, US law has required an imported prescription drug to meet the same requirements as one made domestically, including prior approval of a new drug application by the Food and Drug Administration (FDA).

Recently, however, price differentials between the US and its neighbours have led to calls for new legislation and widespread flaunting of the law by US citizens who, unhappy with the comparatively high prices, are seeking to obtain drugs from foreign sources. As a result, Congress is now considering enacting legislation in this area.

This article considers:

- How parallel trade is regulated in the EU, including the impact of intellectual property and competition laws.
- The recent development of parallel trade in the US, including an explanation of the current legal framework, the efforts of citizens to circumvent the rules, the public health and legal issues raised, and the debate over statutory change.

PARALLEL TRADE IN THE EU

In the EU, parallel trade means the export by a third party of an authorised product from one member state and the placing on the market of that product in another member state without going through a second marketing authorisation procedure. Usually, this will be because there is an identical, or almost identical, local product in the member state of import and the regulatory authorities are able to presume conformity of the imported product with the same standards. The theory is that the parallel import may be placed on the market in the country of import under the umbrella of the full authorisation granted to the equivalent product placed on that market by the originator.

The EU regulatory regime

Before a medicinal product may be placed on the market in the EU, it is necessary to obtain a marketing authorisation. This will usually involve submitting a detailed dossier demonstrating the safety, quality and efficacy of the product (with limited derogations for generic copy products).

In the EU, the authorisation will either be:

- A marketing authorisation granted by one of the national regulatory authorities in accordance with Directive 2001/83/EC. This only permits the product to be marketed in that member state. There is no automatic system of mutual recognition. Any person seeking to export the product would need to obtain a separate market authorisation in the member state of import and submit a dossier containing detailed information relating, for example, to the manufacture of the product.
- A centralised marketing authorisation in accordance with Regulation 2309/93/EC, permitting marketing throughout the EU (*Regulation 726/2004/EC with effect from November 2005*). Such a product may be purchased in one member state for sale in another, but the product information (label and package leaflet) must be in the official language of the member state of sale. Therefore, cross-border distribution will normally involve some level of re-packaging. In some member states, it may also be necessary to change the pack size (to comply with local reimbursement rules).

Parallel importation of nationally authorised products

A parallel importer will not have access to the detailed manufacturing and safety/efficacy data required to obtain a national marketing authorisation. However, through the application of EU principles on free movement of goods, the strict regulatory rules have been mitigated by case law of the European Court of Justice (ECJ) (*in particular, De Peijper (C-104/75) and subsequent cases*), two Commission Communications (*Commission Communications 06.05.1982 and 30.12.2003*) and national administrative provisions.

The effect of these provisions is that, where the information necessary for protecting public health is already available from another source and where other conditions are satisifed, a parallel importer may apply for a special form of licence. Such licence is not granted under Directive 2001/83/EC, but under the general principles of EC law governing free movement of goods (*Articles 28-30, EC Treaty*).

In these circumstances, instead of requiring the parallel importer to submit a dossier demonstrating the safety, quality and efficacy of the product, the regulatory authority in the country of import

must seek this information from other sources. In particular, it will look at:

- Information it already has or can seek from the marketing authorisation holder in relation to the locally authorised product.
- Information which it can obtain from the regulatory authority in the exporting country on the product to be imported.

To be able to import a product, the parallel importer must satisfy the regulatory authority that:

- The product is to be imported from another EU or EEA member state. This is an absolute requirement. (There will be some temporary restrictions in operation in relation to eight of the ten new member states that joined on 1 May 2004. These are linked to the availability of effective intellectual property protection in those member states.) It is not possible to take advantage of the rules if the product is imported from outside the EU or EEA.
- The product to be imported has a marketing authorisation granted under EC law in the exporting member state. Again, this is an absolute requirement.
- The local product and imported product therapeutically have the same effects, but they need not be identical. The most recent case has stated that the test is whether the products are "substantially identical" (*Kohlpharma GmbH v Bundesrepublik Deutschland, Case C-112/02*). However, to the extent that products are not identical, there must be no safety concerns raised by the differences. Recent case law has expanded the scope of parallel importation and the current position is that products may have different excipients and/or different pharmaceutical forms, provided that, in the opinion of the competent authority in the country of import, no safety concerns are raised by the presence on the market of two non-identical products.

Common origin. Until April 2004, the case law also required the parallel importer to satisfy the regulators that there was a link between the manufacturer of the local product and the imported product, either because they were companies in the same group, or licensed the product from a common licensor ("common origin"). However, this requirement appears to have been removed as a result of the recent ECJ decision in the *Kohlpharma* case (*see above*). In that case, there was a common source of the active ingredient, but no other relationship between the marketing authorisation holders in the importing and exporting member states. The court held that, although evidence of a link between the two marketing authorisation holders was helpful in suggesting that the products might be substantially identical, it was not essential.

This case is likely to lead to uncertainty and potentially an increase in the scope for parallel trade, as it blurs the distinction between the rules on marketing authorisations for generic products (cross-referring to the originator's data under Directive 2001/83/EC in the country of import) and the rules governing parallel importation of the same product (on the basis that it is essentially similar to the innovator's product already authorised in the market). Specifically, it might be taken to allow the import of a generic product from one country, where the data protection period has expired, into a country where it has not expired, but where essential similarity with the originator's product can be demonstrated. Such a parallel import would, therefore, undermine the effect of the data protection rules.

The effect of the domestic authorisation being surrendered. Another trend in the case law has been to allow the parallel importation of a product to continue even though the local reference product is no longer on the market in the member state of import, provided there are no risks to public health (*Paranova Läkemedel AB and others v Läkemedelsverket, Case C-15/01; Paranova Oy, Case C-113/01*).

To date, there have been no cases where the reference product has been withdrawn but not replaced by a related product. It remains to be seen how the regulators would react in such a case.

Advance notice. A recent legislative amendment requires the parallel importer to give advance notice to the marketing authorisation holder and regulatory authority in the country of import (*Directive 2004/27/EC, amending Directive 2001/83/EEC; Article 76 of the amended Directive*). Member states are required to implement this requirement by the end of October 2005.

Parallel importation of centrally authorised products

The parallel distributor will not need any additional marketing authorisation to place centrally authorised products on the market in another member state (but it will need a manufacturer's authorisation if it is involved in any re-labelling or packaging).

The European Medicines Evaluation Agency (EMEA) operates a procedure under which a distributor is requested to give three months' notice to the EMEA before commencing the parallel distribution of a specific medicinal product and to provide information about its proposed activities (including details of the product and any re-packaging). The EMEA then checks the conformity of the proposed packaging and responds to the distributor within 30 days. However, there is no legal basis for this procedure in Regulation 2309/93/EC and the EMEA cannot enforce compliance. Under the new provisions to be introduced by Regulation 726/2004/EC next year, the supervisory role of the EMEA will be strengthened, but it will still not have the power to impose sanctions directly. (*See also box, EC competition law and parallel trade.*)

THE IMPACT OF INTELLECTUAL PROPERTY LAW ON PARALLEL TRADE IN THE EU

In the past year there have been a number of decisions in this area by the ECJ, the European Free Trade Association (EFTA) court and the English High Court, of particular relevance to the pharmaceutical sector. They concern the right of the brand owner to object to goods that have been re-packaged or over-labelled.

Exhaustion of rights

The idea of exhaustion is that once a product has been put on the market by the IP owner, or with its consent (*see below*), the IP

owner cannot stop the product being resold in that market by using its IP rights. Most European disputes between brand owner and importer highlight that there is a lack of certainty as to the point at which IP rights are exhausted. The principle has been extended to other forms of intellectual property. In the case of patents, the courts have ruled that first sale gives rise to intra-Community exhaustion (*Case 187/80 - Merck v Stephar*). In the case of copyright, while some rights are not exhausted on first sale, the only really significant copyrights, as far as pharmaceutical companies are concerned, cannot be used. Since 1999, it has been clear that a company would have difficulty in relying on the copyrights in the approved text of its patient information leaflets (or Summary of Product Characteristics (SPC)), as to do so would probably be treated as anti-competitive (*Case E-1/98 (EFTA) - Norwegian Government v Autra Narge, AS*).

Exhaustion can be split further depending on what is considered to be the relevant market. If the market is the EEA, the IP owner's rights are spent once the product is on sale in one of the EEA countries. If, however, the market is the world, the rights are spent once the product is on sale anywhere in the world (the theory of international exhaustion). However, EC law does not recognise the concept of international exhaustion (*Case C-355/96 - Silhouette International Schmied Gmbh Co KG v Hartlauer Handelsgesellschaft GmbH [1998] ECR I-4799*).

Consent

The issue of demonstrating consent is relevant to both non-EEA- and EEA-sourced parallel imports. Consent can be express or implied. If implied, the circumstances must show that the brand owner unequivocally demonstrated that it had renounced its rights (*C-414 to 416/99 – Davidoff*). The consequence of this is that all non-EEA-sourced goods are effectively infringing, unless evidence of brand owner consent can prove them to be lawful.

It can sometimes be difficult for the importer to tell if consent has been given, or for the brand owner to prove that it has not. The issue of identification can be a difficult one, complicated by European competition rules. For example, in some circumstances, an importer can remove product codes, on the basis that batch codes may force it to reveal its source and there may be risk of market partitioning if sources are revealed (*C-349/95 - Loendersloot v Ballantine; and C-244/00 - Van Doren*).

In December 2003, Glaxo announced that it was going to colour certain anti-retroviral drugs intended to be sold in developing countries. Its decision was preceded by an English case that illustrated some common problems associated with products destined for developing countries (*Glaxo Group Limited v Dowelhurst Limited and Richard Taylor (Anti-retrovirals and Africa), High Court of Justice, Chancery Division, Peter Prescott QC (Sitting as a Deputy Judge), 31 July 2003*). Glaxo's products were packaged in standard, EMEA approved packaging. There were no stickers, warnings or colour changes which would indicate that the goods were only for sale in non-EEA countries. Glaxo intended the products to be supplied to Africa, but they were diverted to a Swiss company, and eventually appeared in the UK. Glaxo sued for trade mark infringement.

The case has yet to reach trial, but at an interim hearing the English Court of Appeal commented as follows:

"If the defendant cannot tell whether goods are or are not in free circulation then an absolute injunction may put him in real difficulty…[it] may have the practical effect of impeding inter-State trade. A lot might therefore depend on how readily one can distinguish between goods from outside and those from inside the EEA. This may include how readily the trade mark owner is prepared to co-operate in such identification" (*Glaxo Group Limited v Dowelhurst Limited and Richard Taylor (Anti-retrovirals and Africa), Court of Appeal (Civil Division), Lord Phillips of Maltravers, Lord Justice Tuckey, Lord Justice Jacob, 15 March 2004 [2004] EWCA (Civ) 290*).

The decision leaves much unresolved, but the message for manufacturers is that goods destined for non-EEA countries should be clearly marked as such.

Re-packaging and re-labelling

The ECJ's decision in *Glaxo/Boehringer* is the most significant of the cases which have sought to reconcile the tension between protecting a company's trade mark rights and ensuring the free movement of goods throughout the EU. The cases seek to reach a balance on the appropriate interpretation of Articles 7(1) and 7(2) of the Trade Marks Directive (*see also Hoffmann-La Roche v Centrafarm (Case 102/77 [1978] ECR 1139); Bristol-Myers Squibb and Others v Paranova (Joined Cases C-427/93, C-429/93 and C-436/93 [1996] ECR I-3457); Loendersloot v Ballantine (Case C-349/95); and Upjohn v Paranova (Case C-379/97 [1999] ECR I-6927)*). But, much is still unclear.

The essence of the current ECJ case law is that an importer who re-packages and re-applies a trade mark will infringe, unless it satisfies all five of the following conditions:

- It is "necessary" to re-package to effectively market the product in the importing country.
- The re-packaging has no detrimental effect on the original condition of the product and proper instructions are included.
- There is clear identification of the manufacturer and the importer.
- The presentation of the re-packaged goods causes no harm to the trade mark.
- Proper notice is provided.

These conditions are all about protecting the reputation of the mark. A fair summary of the present position is that re-affixing the mark creates a risk of jeopardising the reputation; but, if the above conditions are satisfied, that risk is treated as removed.

Necessity to re-package. The ECJ has said that the test is whether the circumstances prevailing at the time of marketing in the importing member state made re-packaging "objectively necessary". A trade mark owner would not be justified in objecting to such re-packaging if it hindered effective access of the imported product to the market of the member state. For example, the ECJ has accepted that there could be cases where there was such a strong resistance to re-labelled products that re-packaging would be required in order to achieve effective access

EC COMPETITION LAW AND PARALLEL TRADE

The two main competition law provisions of the EC Treaty relevant to restrictions on parallel trade are Articles 81 and 82. Article 81(1) prohibits agreements and practices that restrict competition (and affect trade between member states), unless they meet the conditions to benefit from the exception set out in Article 81(3). Article 82 prohibits an undertaking abusing its dominant position.

Based on the European Commission's (the Commission) practice to date, the basic rule so far has been that, under Article 81, agreements that limit parallel trade are unlawful. The common rationale advanced for this per se rule is that restrictions to parallel trade hinder the basic objective of market integration contained in the EC Treaty. The Commission explained its thinking, in relation to a dual-pricing policy, in the Spanish *GlaxoWellcome* case, currently on appeal before the European Court of First Instance (CFI).

However, recent case law from the CFI and the European Court of Justice (ECJ) clarifies the conditions under which Article 81 is applicable to certain types of behaviour that limit parallel trade. The CFI's case law in particular contains helpful statements on the extent to which Article 81 can be applied as a policy tool. This clarification will potentially have significant consequences for the relationship between EC competition law and parallel trade (*see below, Article 81*).

The application of Article 82 to practices aimed at limiting parallel trade is less developed in the Commission's practice and no precedents exist in EC case law. Some of the main issues that remain to be clarified include the definition of the relevant market and the concept of dominance. These give rise to interesting questions, in particular in light of governmental price regulation in pharmaceutical markets.

Article 81

Article 81 applies to agreements and concerted practices between undertakings, but not to an undertaking's unilateral behaviour. The criteria to be met for an agreement to exist, and the conditions under which such criteria are considered fulfilled, are crucial when establishing the limits within which a supplier may legally manage its supply chain.

The recent CFI and ECJ judgments in the *Bayer* case shed light on these questions (*Joined Cases C-2/01 P and C-3/01 P, Bundesverband der Arzneimittel-Importeure v Bayer and Commission*). In particular, the judgment:

- Significantly increases the burden of proof on the Commission in showing that an agreement exists based on a concurrence of wills or tacit acquiescence and provides useful guidance on the circumstances that will be relevant, particularly in the pharmaceutical sector, in concluding the absence of an agreement (*see below*).
- Provides that there is no basis in case law for a general prohibition under Article 81 of the EC Treaty on preventing parallel trade. The CFI stated more specifically that it is not open to the Commission to attempt to achieve results such as price harmonisation and market integration by straining the scope of Article 81. (Depending on the specific circumstances of a case, there may be scope for applying the exceptions under Article 81(3) even to agreements that have as their object or effect the restriction of parallel trade.)

The *Bayer* case. The case concerned the French and Spanish pharmaceutical markets in which, as a result of price regulation, Bayer's Adalat drug was, on average, 40% cheaper compared to the UK. Parallel importers exported large quantities of the drug from France and Spain to the UK and, according to Bayer, caused the company to lose DM100 million (about EUR51 million) in annual income. As a result, Bayer's subsidiaries in France and Spain decided to reduce their supplies to wholesalers to the level of their domestic needs plus 10%.

Before the CFI (and the ECJ on appeal), it was established that Bayer did not in any way seek its wholesalers' co-operation. Wholesalers also strongly objected to the adopted measures and tried to circumvent them. Bayer did not systematically monitor the destination of the products ordered by the wholesalers and the exporting wholesalers were not identified or penalised. Finally, supply quotas were set *ex ante* and applied without discrimination.

Guidance on when an agreement exists. The ECJ supported the CFI decision against the Commission and found that no concurrence of wills and no tacit acquiescence could be demonstrated. Therefore, it overturned the Commission's finding that Bayer's behaviour stemmed from contractual relations with the wholesalers. In particular, the ECJ found that:

- The wholesalers did not share Bayer's intention to prevent parallel imports.
- There was no invitation (express or implied) to fulfil an anti-competitive goal jointly.
- Bayer's actions were an expression of a unilateral policy that could be put into effect without assistance.

It also stated that the wholesaler's continuation of their business relations is not a sufficient basis to establish a concurrence of wills or tacit acquiescence.

Article 82

With the *Bayer* judgment, the Commission's practice of applying a very restrictive interpretation to the concept of unilateral behaviour (and including within the scope of Article 81 a wide range of practices which *a priori* seem entirely unilateral) has suffered a severe blow. It may be expected that, in the future, Article 82 will play a more prominent role in the attempt to limit practices that restrict parallel trade.

Article 82 governs abusive behaviour by a dominant undertaking. Three questions arise in relation to this section:

- How the relevant market should be defined when assessing practices that limit parallel trade (*see below*).
- Whether the undertaking concerned can be considered to be dominant.
- What type of behaviour is likely to be abusive and, in particular, whether hindering parallel trade is abusive per se (*see below*).

Market definition. Dominance on the part of an undertaking is intrinsically linked to the definition of the relevant market. In the area of pharmaceuticals, there is no guidance in case law on market definition for the purposes of applying Article 82 and guidance in Article 81 case law is limited. There is, however, significant guidance in EU merger control.

Broadly, the approach adopted by the Commission in merger control cases is based on therapeutic use substitutability, generally by grouping products at the third level of the Anatomical Therapeutic Chemical (ATC) classification. However, this approach may be less appropriate from the parallel traders' point of view, since the determining factor for these traders is rarely therapeutic use, but rather the scope for price arbitration between countries.

Based on this line of argument, some legal commentators have suggested that the relevant market should be defined as the group of all prescription medicines that can profitably be parallel traded (*see Fréderic Jenny, Pharmaceuticals Competition and Free Movement of Goods, paper presented to the Hellenic Competition Authority's EU Competition Law and Policy Conference on 19 April 2002*). Others argue that each drug may constitute a separate relevant market (*see Case C-53/03 SIFAIT v GlaxoSmithKline, currently pending before the ECJ upon preliminary reference from Greece*). However, this latter approach appears untenable if parallel traders are considered to constitute the relevant demand level.

Abusive behaviour. The next question is whether an attempt to limit export sales is a per se abuse. There is no EC case law on the issue, but statements by the CFI in the *Bayer* case suggest that such a per se rule does not exist (a position which also seems to be supported by the Commission).

Assuming that restrictions on parallel trade are not a per se infringement, the question arises of how they should be assessed. Often, such restrictions will take the form of refusals to supply or limitations on quantities supplied. Guidance is available in EC case law on refusals to supply/license (*see for example, Joined Cases 6 and 7-73, Istituto Chemioterapico Italiano S.p.A. and Commercial Solvents Corporation v Commission, Case C-7/97, Oscar Bronner GmbH & Co. KG v Mediaprint Zeitungs- und Zeitschriftenverlag GmbH & Co. KG and Case C-418/01, IMS Health v NDC Health*).

Exceptional circumstances must be present for a refusal to supply to be abusive. If the refusal affects an existing customer:

- The supplier must be the only source of supply.
- The refusal must have the effect of creating an immediate and substantial competitive disadvantage for the customer.
- The refusal must threaten to eliminate competition.
- The refusal cannot be objectively justified.

If the refusal does not affect an existing customer, the essential facilities doctrine applies and a refusal will only be an abuse if:

- The product concerned is an indispensable input to operate on a downstream market.
- The refusal eliminates competition on that market.
- The refusal cannot be objectively justified.

Both approaches are based on the principle that dominant companies are not under any general obligation to deal with customers on terms, or by supplying quantities, that are against their interests. On the contrary, dominant undertakings may also legitimately pursue profit-maximisation. It is therefore suggested that the conditions set out in the general case law, as briefly illustrated above, should equally apply to parallel trade cases in the pharmaceutical sector, and that the legality of the behaviour should not depend on the customer's intention to export or not. Ultimately, what is likely to play a determining role is the effect on consumers that the behaviour creates and parallel trade is not generally recognised as creating material benefits for consumers.

There will soon be guidance available on the application of Article 82, when the ECJ rules on the preliminary questions raised in the *SIFAIT v GSK* case.

to the market (in other words, it would be objectively necessary in practical terms, if not in legal terms). One English judge has said that a strong resistance from a significant proportion of consumers would be enough to count as a hindrance.

Conflicting opinions on the test of objective necessity. Views vary greatly across the EU on the ECJ's necessity test.

One view is that it applies not only to re-packaging, but also to the details of the manner of re-packaging (*Orifarm v AstraZeneca Danish Supreme Court, 4 January 2002; Eurim-Pharm v Boehringer Ingelheim Federal Supreme Court of Germany, 11 July 2002; Schuber Verpacking II, Austrian Supreme Court, 30 January 2001; Glaxo Group Limited & Others v Dowelhurst Limited and Swingward Limited English High Court, 6 February 2003; and the Swedish Court of Appeal has taken a similar view in a brief interlocutory decision, Beecham v Netpharma, 16 April 2000*). If this test is correct, parallel importers and courts would be placed in an awkward position, as they would need to decide when a particular packaging design was unnecessary.

The other view is that the necessity test applies to the act of re-packaging, not to the presentation of the re-packaged product. The owner may oppose the presentation of the products if it is liable to damage the trade mark (*Case - E-3/02 Paranova AS v Merck & Co., Inc. and Others, EFTA court (8 July 2003); Norwegian Supreme Court (case number 2002/5082); and the European Commission (the Commission) also supports this view*).

The two views are diametrically opposed, and in March 2004 an English court referred the *Glaxo/Boehringer* case back to the ECJ (*Glaxo Group v Dowelhurst English Court of Appeal, 5 March 2004*). The reference will inevitably delay the resolution of other similar cases.

Accession derogation

On 1 May 2004 ten new countries joined the EU. The Accession Treaty includes an exception to the general rule on exhaustion of rights in the EEA in relation to eight of them (Czech Republic, Slovakia, Hungary, Poland, Slovenia, Latvia, Lithuania and Estonia) (the EU8 countries). In particular, the IP owner can block the import of a product if:

- The product is being exported from one of the EU8 countries; provided that
- The IP owner is the owner of a patent or SPC in the destination EEA country; and
- The product could not previously have obtained equivalent patent protection in the EU8 exporting country, in other words, at the time the patent/SPC was filed in the EEA country.

Significantly, the provision applies whether consent exists or not. The normal rule of intra-Community exhaustion does not apply. It does not matter if an IP owner placed the goods on the market in the EU8 country – it can still stop them from being exported from an EU8 country to another EU state.

In addition, the importer must demonstrate to the regulatory authority in the importing country that it has given one month's notice to the local patent/SPC holder (not a related company) of its intention to import the goods. This notice provision came from a suggestion by European Federation of Pharmaceutical Industry Associations (EFPIA) that the patent holder be given a limited period in which to object to the grant of any import licence.

To date, there has been no publication concerning any firm agreement in the UK, or any other member state, as to the notification procedure. It has been suggested by some commentators that any notice will need to include the following:

- Information concerning active ingredient, pack size, dose, and so on.
- When and where the trader obtained the product.
- When and where it intends to put it on the market.

However, no announcement from the Commission or a regulatory authority has suggested that a comprehensive notification is required.

Member states were expecting guidance from the Commission on the subject of the proper form of notice. The competent authority in the UK has now developed its own procedure, having consulted informally with industry groups (including parallel importers). It proposes to require the importer to do the following, and nothing more: provide the date on which the notification was given to the holder or beneficiary of the patent/SPC, treating the marketing authorisation holder as the beneficiary. If this obligation has been fulfilled (and the other conditions for grant of a parallel import licence are satisfied), then the approval will be issued.

PARALLEL TRADE IN THE US

Currently, no prescription drugs can be imported into the US without being in full compliance with requirements for labelling, quality and an approved New Drug Application (NDA). However, in recent years, US citizens have become dissatisfied with the comparatively high prices and have been obtaining drugs from foreign sources. This has led US policy-makers to examine the possibility of lowering the current barriers to importation of prescription drugs.

Current US law governing importation of prescription drugs

Beginning in 1938, the Federal Food, Drug, and Cosmetic Act prohibited the movement of "new drugs" in "interstate commerce" without an NDA in effect (*21 U.S.C. 331(d), 355(a)*). Interstate commerce includes not only trade between two states within the US, but also trade with foreign countries. Therefore, any prescription drug imported into the US must also have FDA approval of an NDA.

The NDA requirement is exceptionally broad. After many court decisions and administrative actions, virtually every prescription drug is subject to the NDA requirement. Also, the agency succeeded in establishing the principle that each distinct product required its own NDA, so that generic versions of approved products were required to obtain separate approvals. Each NDA contains, in addition to pre-clinical and clinical safety and effectiveness data, extensive descriptions of the manufac-

turing processes and controls. Any subsequent alteration or improvement in these processes and controls (with a few minor exceptions) must also be reviewed and approved by the FDA. The elaborate regulatory framework assures that each prescription drug has met appropriate standards to protect consumers.

The statutory protections of the NDA requirement are reinforced under the Federal Food, Drug, and Cosmetic Act by provisions prohibiting the adulteration (*see below*) or mis-branding of a drug. Adulteration can occur if, for example, a drug is not produced in conformity with current Good Manufacturing Practices (*21 U.S.C. 351(a)(2)(B)*), or it fails to meet the standards of the US Pharmacopeia (*21 U.S.C. 351(b)*). A drug may be mis-branded under a wide range of circumstances, such as when it fails to bear adequate directions for medical use as approved under an NDA (*21 U.S.C. 352(f)*).

To protect consumers, the law has special procedures for imported drugs. When a drug is presented to customs officials, the FDA is supposed to be notified and permitted to examine the product. If it appears to be adulterated or mis-branded, or not covered by an approved NDA, the FDA may direct customs to refuse admission of the goods (*21 U.S.C. 381(a)*). During the 1980s, the FDA uncovered several situations in which prescription drugs were being imported on the basis that they had been made under an NDA and exported from the US, and so met the statutory requirements. On examination, the products were found to be counterfeit. In 1987, Congress amended the Federal Food, Drug, and Cosmetic Act to prohibit the importation of prescription drugs made in the US by anyone other than the manufacturer (*21 U.S.C. 381(d)*).

The current legal framework is designed to seal US borders from unapproved prescription drugs. In 2000, Congress enacted a provision that would permit the importation of prescription drugs into the US, provided that the Secretary of Health and Human Services certified that such importation would not present safety problems and would result in savings to US consumers (*21 U.S.C. 384*). Neither Secretary Donna Shalala (President Clinton's appointee) nor Secretary Tommy Thompson (President Bush's appointee) would make the necessary certification, and so the law has not been implemented.

Also, in 2003, Congress directed the United States Department of Health and Services (HHS) to undertake a review of the safety and economic effects of drug imports and that study is underway. Without waiting for this report, the US Senate began examining, in the spring of 2004, several bills that would lower the current barriers to importation of prescription drugs (*see box, US legislative issues*).

The FDA has permitted one broad exemption to this general rule. As a matter of enforcement discretion – not legal right – individuals are allowed to bring into the US limited supplies of unapproved drugs for personal use. The policy, adopted during the early days of the AIDS epidemic when no therapies were yet approved, applies principally to drugs for serious medical conditions for which effective treatment is not available in the US (*FDA Regulatory Policy Manual, Chapter 9, Subchapter on Coverage of Personal Importations, available at www.fda.gov/ora/compliance_ref/rpm_new2/ch9pers.html*). It does not cover prescription drugs that are already approved by FDA. It also excludes controlled substances and products that represent health risks or fraudulent schemes.

US LEGISLATIVE ISSUES

Recently, the US Senate began examining several bills that would lower the current barriers to importation of prescription drugs. The policymakers face a number of difficult questions, such as:

- Will only drugs made in US be allowed to be imported? Or will similar drugs – containing the same active ingredients, but not identical to the FDA-approved product – be permitted as well? If the latter, how different may the drugs be from that approved by the FDA?
- Should some categories of drugs not be imported? Current legislative proposals would exclude controlled substances, biologics and drugs for intravenous administration.
- Can products be imported from anywhere or only from certain countries?
- Will imports be limited to consumers, or may wholesalers and retailers also be allowed? This question will have a considerable impact on competition among commercial operators and on how any savings that imports create will be shared.
- Will foreign suppliers to the US market be regulated and inspected by the FDA?
- Once some drugs can be lawfully imported, how will the drugs that cannot be imported be excluded from the US market?

Price differentials and citizen revolt

The US does not impose price controls on prescription drugs, unlike most other countries. Its policy prefers competition and incentives for new product development. This, combined with the wealth and income of the country, has resulted in prices that can be significantly higher than in other countries.

Beginning in the late 1990s, many senior citizens went to Canada (and to a lesser extent Mexico) to get prescriptions made up at cheaper prices. Some politicians helped organise these trips and there was significant press coverage. The internet offered another way to order prescription drugs from overseas. Websites offering drugs at Canadian prices appeared. The Governor of the State of Minnesota set up a website for his citizens that linked directly to selected Canadian pharmacies. He has also encouraged state employees to get their drugs through this route, in order to reduce state insurance costs. Governors in Wisconsin, New Hampshire, Vermont and Illinois are working on similar ideas to gain access to lower-priced drugs from outside the US.

Also, US-based businesses have sought to create their own opportunities. For example, one Arkansas pharmacy set up a relationship with a pharmacy in Canada to supply its customers

with drugs from Canada. Another business bought drugs in bulk and re-packaged them for sale in the US.

The result is that the FDA now estimates that 200,000 packages containing prescription drugs are coming into the US every week intended for consumers.

Risks presented by current imports

The FDA has expressed concern about the safety of the products being imported, since it does not believe that the drugs are generally what they claim to be. It has carried out several undercover operations to buy products over the internet and sites that claimed to be located in Canada were found to supply drugs from the Far East, Africa or the Caribbean. In addition, the FDA and customs have made intensive examinations of drugs offered for import. The results are discouraging. The FDA found, among other things (*see www.fda.gov/importeddrugs*):

- Counterfeit products – some harmless, some contaminated.
- Therapeutic moieties never approved by the FDA or withdrawn from the US market.
- Animal drugs not authorised for use in humans.
- Unapproved generic versions of drugs with no supporting evidence of therapeutic equivalency.
- Products not labelled in English, or missing vital information required in US products.
- Improperly packaged drugs, subjecting them to contamination, degradation and damage.
- Products from batches that had been recalled for quality or safety reasons.

One important difference between parallel trade in the EU and the importation to the US involves drug packaging. In North America, most solid oral dosage form products are distributed in large volume packages, which are then re-packed by pharmacists for dispensing to consumers. This means that most consumers will receive drugs in containers other than the one packaged by the original manufacturer. The opportunities to substitute defective, damaged, outdated, diluted or counterfeit products are greatly helped by this practice. Sophisticated counterfeiting of original manufacturer packaging is also on the increase.

Legal issues presented by current imports

Because drug importation by wholesalers, retailers and consumers is illegal, no case law has yet developed on issues regarding competition, intellectual property protection and product liability. However, in the last six months, numerous global pharmaceutical companies have begun to take steps to reduce the flow of their products from Canada into the US. These actions include:

- Contractual limits on resale out of Canada.
- Certifications that sales are domestic.
- Quotas on the volume of drugs that are supplied from the manufacturer.

Predictably, litigation is now emerging in the US alleging that these restrictions breach US anti-trust laws by restraining trade in prescription drugs. In a preliminary motion, one company argued that, since the trade in this instance (importation of drugs from Canada except as permitted by the FDA) was completely illegal, its actions merely furthered an existing statutory ban. The court was not persuaded that the prohibition of imports was absolute, but said that, in any event, it was not up to the company to enforce that law. Therefore, it refused to rule that there could not be an anti-trust violation. This matter is still in the early stages of litigation. In addition, there are some consumer class actions that have recently been filed claiming that large pharmaceutical manufacturers had conspired to prevent competition in the US by limiting supplies to Canada.

The advocates of importation from Canada are also just beginning to recognise the patent, trade mark and copyright issues that have been litigated extensively in the EU. Undoubtedly, if drug importation itself is legalised, the US will see similar issues raised. For example, Canada has a law that permits compulsory cross-licensing of patents under certain circumstances. If this law were invoked, the question arises of whether the generic versions so authorised would be importable or excluded by US patent law.

In the US, product liability laws may also become relevant in this area and companies doing business there may face significant exposure for injuries arising from imported drugs. In particular:

- Consumers may not be able to sue the foreign supplier at all, or have US laws apply to the foreign entity, or collect any judgment.
- The consumer will believe that the medicine he took was actually made by the US business. Yet, given the potential for counterfeit, damaged, outdated or diluted products, the consumer may not have received what the manufacturer originally made, and there may be no samples left to test.
- The manufacturer may also be charged with failing to take adequate steps to prevent the counterfeiting, dilution or other misconduct by intermediaries.
- If the jury awards damages against both the US company and a foreign supplier, the court can compel either party to pay 100% of the amount, even if it were only 1% responsible for the injury in question.