**European Court of Justice, 16 December 1999, Rhone-Poulenc Rorer and May & Baker**

**PHARMACEUTICAL LAW – FREE MOVEMENT OF GOODS**

**Parallel imports**

- **If medicinal product X has the same active ingredients and therapeutic effect as medicinal product Y, but does not use the same excipients and is manufactured by a different manufacturing process, where the competent authority in Member State B is in a position to verify that medicinal product X complies with the requirements relating to quality, efficacy and safety in normal conditions of use and is in a position to ensure normal pharmacovigilance, a parallel import licence can be seeked and obtained without complying with all the requirements of the Directive.**

That where it is sought to import medicinal product X from Member State A into Member State B, it is permissible for the person who proposes to place the imported product upon the market in Member State B to seek and obtain a parallel import licence from the competent authority in Member State B:

— medicinal product X is the subject of a marketing authorisation granted in Member State A and was the subject of a marketing authorisation which has ceased to have effect in Member State B;

— medicinal product Y is the subject of a marketing authorisation granted in Member State B, but is not the subject of a marketing authorisation granted in Member State A;

— medicinal product X has the same active ingredients and therapeutic effect as medicinal product Y, but does not use the same excipients and is manufactured by a different manufacturing process, where the competent authority in Member State B is in a position to verify that medicinal product X complies with the requirements relating to quality, efficacy and safety in normal conditions of use and is in a position to ensure normal pharmacovigilance;

— the marketing authorisations referred to above were granted to different members of the same group of companies and the manufacturers of medicinal products X and Y are also members of that group of companies; and

— companies within the same group as the holder of the marketing authorisation for product X which has been withdrawn in Member State B continue to manufacture and market product X in Member States other than Member State B.

In such a situation, the competent authority is not required to take into consideration the fact that medicinal product Y was developed and introduced in order to provide a particular benefit to public health which medicinal product X does not provide and/or that that particular benefit to public health would not be achieved if product X and product Y were both on the market in Member State B at the same time.

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**European Court of Justice, 16 December 1999**
(G.C. Rodríguez Iglesias, D.A.O. Edward, L. Sevón, R. Schintgen , C. Gulmann , J.-P. Puissochet, G. Hirsch, P. Jann and H. Ragnemalm)
JUDGMENT OF THE COURT
16 December 1999 (1)
(*Medicinal products — Marketing authorisation — Parallel imports*)
In Case C-94/98,
REFERENCE to the Court under Article 177 of the EC Treaty (now Article 234 EC) by the High Court of Justice of England and Wales, Queen's Bench Division, United Kingdom, for a preliminary ruling in the proceedings pending before that court between
The Queen
and
The Licensing Authority established by the Medicines Act 1968
(represented by the Medicines Control Agency),
ex parte: Rhône-Poulenc Rorer Ltd,
May & Baker Ltd,
on the interpretation of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products (OJ, English Special Edition 1965-1966, p. 20), as amended, in particular, by Council Directive 93/39/EEC of 14 June 1993 (OJ 1993 L 214, p. 22), and of the provisions of Community law relating to the grant of parallel import licences for medicinal products,
THE COURT,
composed of: G.C. Rodríguez Iglesias, President, D.A.O. Edward, L. Sevón, R. Schintgen (Presidents of Chambers), C. Gulmann (Rapporteur), J.-P. Puissochet, G. Hirsch, P. Jann and H. Ragnemalm, Judges,
Advocate General: A. La Pergola,
Registrar: D. Louterman-Hubeau, Principal Administrator,
after considering the written observations submitted on behalf of:
— Rhône-Poulenc Rorer Ltd and May & Baker Ltd, by G. Hobbs QC and J. Stratford, Barrister, instructed by R. Freeland and M. Farquharson, Solicitors,
— the United Kingdom Government, by J.E. Collins, Assistant Treasury Solicitor, acting as Agent, assisted by R. Drabble QC and P. Saini, Barrister,
— the French Government, by K. Rispal-Bellanger, Head of Subdirectorate in the Legal Affairs Directorate of the Ministry of Foreign Affairs, and R. Loosli-Surrans, Head of Mission in that directorate, acting as Agents,
— the Commission of the European Communities, by R.B. Wainwright, Principal Legal Adviser, and H. Støvlbæk, of its Legal Service, acting as Agents,
having regard to the Report for the Hearing,

after hearing the oral observations of Rhône-Poulenc Rorer Ltd and May & Baker Ltd, represented by G. Hobbs and J. Stratford, of the United Kingdom Government, represented by R. Drabble and P. Saini, of the French Government, represented by R. Loosli-Surrans, of the Swedish Government, represented by A. Kruse, Departementsråd in the Legal Affairs Secretariat (EU) of the Ministry of Foreign Affairs, acting as Agent, and of the Commission, represented by R.B. Wainwright and H. Støvlbæk, at the hearing on 9 March 1999,
after hearing the **Opinion of the Advocate General** at the sitting on 19 May 1999,
gives the following
**Judgment**
1. By order of 31 July 1997, received at the Court on 1 April 1998, the High Court of Justice of England and Wales, Queen's Bench Division, referred to the Court for a preliminary ruling under Article 177 of the EC Treaty (now Article 234 EC) two questions on the interpretation of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products (OJ, English Special Edition 1965-1966, p. 20), as amended, in particular, by Council Directive 93/39/EEC of 14 June 1993 (OJ 1993 L 214, p. 22) ('the Directive‘), and of the provisions of Community law relating to the grant of parallel import licences for medicinal products.
2. Those questions were raised during proceedings between Rhone-Poulenc Rorer Ltd ('RPR‘) and May & Baker Ltd ('M & B‘), and the Licensing Authority established by the Medicines Act 1968, represented by the Medicines Control Agency ('the MCA‘), concerning decisions taken by the MCA on parallel import licences for a medicinal product called 'Zimovane‘.
**The relevant provisions**
3. Article 30 of the EC Treaty (now, after amendment, Article 28 EC) states that quantitative restrictions on imports and measures having equivalent effect are prohibited between Member States. However, Article 36 of the EC Treaty (now, after amendment, Article 30 EC) provides that prohibitions and restrictions on imports between Member States which are justified on grounds of, inter alia, the protection of health of humans are permitted, so long as they do not constitute a means of arbitrary discrimination or a disguised restriction on trade between Member States.
4. Under Article 3 of the Directive, no medicinal product may be placed on the market of a Member State unless an authorisation has been issued by the competent authorities of that State.
5. Article 4 of the Directive defines the procedure, documents and information required in order to obtain a marketing authorisation. Under point 3 of Article 4 of the Directive, an application for a marketing authorisation must be accompanied by qualitative and quantitative particulars of all the constituents of the medicinal product. Under point 8 of Article 4 of the Directive, the application must be, in particular, accompanied by the results of physico-chemical, biological or microbiological tests, pharmacological and toxicological tests, and clinical trials. Under point 9 of the same article, the application must be accompanied by a summary of the product characteristics and one or more specimens or mock-ups of the sales presentation of the medicinal product. Article 4a of the Directive, which was inserted by Council Directive 83/570/EEC of 26 October 1983 (OJ 1983 L 332, p. 1), specifies the information that must be included in the summary of the product characteristics.
6. Article 5 of the Directive provides that the authorisation will be refused if, after verification of the particulars and documents listed in Article 4, it proves that the medicinal product is harmful in the normal conditions of use, or that its therapeutic efficacy is lacking or is insufficiently substantiated by the applicant, or that its qualitative and quantitative composition is not as declared.
7. Article 10 of the Directive provides that authorisation is to be valid for five years and is to be renewable for five-year periods after consideration by the competent authority of a dossier containing details of the data on pharmacovigilance and other information relevant to the monitoring of the medicinal product.
8. Article 29a of Second Council Directive 75/319/EEC of 20 May 1975 (OJ 1975 L 147, p. 13), inserted by Directive 93/39, provides that the Member States are to establish a pharmacovigilance system which, in particular, imposes obligations on the holder of the marketing authorisation in respect of recording and reporting all adverse reactions to the medicinal product. Thus, records must be submitted to the competent authorities at regular intervals and must be accompanied by a scientific evaluation.
9. In 1984, on the basis of a Commission communication published on 6 May 1982 (OJ 1982 C 115, p. 5), which is based on **Case 104/75 De Peijper [1976] ECR 613**, the MCA issued a document entitled 'Notes on Application for Product Licences (Parallel Importing) (Medicines for Human Use)‘ ('MAL 2 (PI)‘).
10. An import of medicinal products is treated as a 'parallel import‘ for the purpose of MAL 2 (PI) where a product is the subject of a United Kingdom marketing authorisation and an applicant wishes to import from the European Community a version of that product which already has a marketing authorisation issued by another Member State. In accordance with MAL 2 (PI), applications for parallel import licences are examined and assessed according to a 'simplified‘ procedure under which the applicant needs to provide less information than is required for an application for a marketing authorisation made in accordance with the Directive.
11. Paragraph 4 of MAL 2 (PI) provides that:
'All the following conditions must be met before an application can be considered under these arrangements i.e. the product concerned must be —
(a) A product which is to be imported from a Member State of the European Community;
(b) a proprietary medicinal product (as defined in Article 1 of EC Directive 65/65) for human use ...;

(c) covered by a currently valid marketing authorisation granted, in accordance with Article 3 of EC Directive 65/65, by the regulatory authority of an EC Member State;
(d) ... have no differences, having therapeutic effect, from a product covered by a UK product licence (PL) ...;
(e) made by, or under licence to:
(i) the manufacturer who made the product covered by the UK product licence or;
(ii) a member of the same group of companies as the manufacturer who made the product covered by the UK product licence.
If any of these conditions is not met the applicant will be invited to apply for a PL in the normal way under the MAL 2 procedures.‘
12. Paragraph 12 of MAL 2 (PI) provides that an authorisation for parallel imports continues in force only so long as both the United Kingdom licence and the Community marketing authorisation to which it relates are in force. If either ceases to be valid for any reason (for example, through expiry or revocation) the parallel import licence also ceases to be valid.
13. Paragraph 21 of MAL 2 (PI) provides that the normal arrangements apply with regard to variations to a parallel import licence made at the request of the licence holder. The licensing authority needs to ensure that the licence is kept in line with the relevant provisions of the appropriate product licence. The licensing authority will notify the parallel import licence holder of any action necessary as the result of a variation to the United Kingdom product licence. The parallel import licence holder is required to notify the licensing authority of any variation to the Community marketing authorisation that comes to his attention. He must seek approval to market the varied product by asking for a variation to that parallel import licence. No batch of a varied product may be marketed in the United Kingdom until the variation has been approved by the licensing authority.

**The main proceedings**

14. In 1989 and 1993, M & B, a member of a group of companies which operate in the research-based pharmaceutical industry, obtained marketing authorisations issued by the MCA covering various forms of tablets and capsules of the product called 'Zimovane‘, which is used for the treatment of insomnia and whose generic name is zopiclone. M & B appointed RPR as its agent to manufacture and market that product.
15. After more than three years of research, RPR developed a new version of Zimovane. It contains the same active ingredients and has the same therapeutic effect as the old version, but is manufactured by a different manufacturing process and using different excipients which provide a particular benefit to public health compared with the old version of Zimovane.
16. RPR submitted the required relevant data to the MCA in order to establish the safety, efficacy and quality of the new version and, on 11 July 1996, the MCA granted a variation to some of the existing marketing authorisations relating to Zimovane. The variations allow RPR to market its new version of Zimovane in the United Kingdom. On 31 July 1996, at the request of RPR, the MCA revoked the authorisations under which the old version of Zimovane had been marketed.
17. Accordingly, RPR has no longer marketed the old version of Zimovane in the United Kingdom. However, RPR continued to market that version of Zimovane in the other Member States, its new version only being marketed in the United Kingdom.
18. Before the authorisations relating to the old version of Zimovane were revoked, parallel import licences for that version were granted to several companies, in accordance with MAL 2 (PI). When the parent authorisation upon which they depended was revoked by the MCA, they lapsed under paragraph 12 of MAL 2 (PI). The holders of the parallel import licences were informed by the MCA that, if they wished to maintain their licences, they had to apply for variations to those licences in order to determine a new appropriate reference product. After examining the applications made to this effect, the MCA, by a number of decisions taken between November 1996 and May 1997, decided to treat the parallel import licences as still valid, those licences then being appended to the marketing authorisation issued for the new version of Zimovane. The MCA also, with effect from 1 August 1996, issued three new parallel import licences for the old version of Zimovane.
19. On 14 February and 5 June 1997, M & B and RPR lodged applications for judicial review of the MCA's decisions claiming that, in the absence of any subsisting marketing authorisations for the old version of Zimovane in the United Kingdom, imports of that version into the United Kingdom were not parallel imports, so it was contrary both to the legislation applicable in the United Kingdom and to Community law to treat them as such.
20. During those proceedings, the MCA contended, in particular, that had it treated the two versions of Zimovane as different products and required the parallel importers of the old version of that product to apply for marketing authorisationsunder the Directive, it would have created an unjustifiable restriction on imports contrary to Article 30 of the Treaty.
21. In those circumstances, the national court decided to stay proceedings and to refer the following questions to the Court for a preliminary ruling:
'1. In a case where medicinal product X is sought to be imported from Member State A into Member State B, is it permissible for the person who proposes to place the imported product upon the market in Member State B to seek and obtain a marketing authorisation from the competent authority in Member State B without complying with the requirements of Council Directive 65/65/EEC (as amended) if:
(a) medicinal product X is the subject of a marketing authorisation granted in Member State A and was the subject of a marketing authorisation which has ceased to have effect in Member State B; and
(b) medicinal product X has the same active ingredients and therapeutic effect as medicinal product Y,

but is not manufactured according to the same formulation as medicinal product Y; and

(c) medicinal product Y is the subject of a marketing authorisation granted in Member State B, but is not the subject of a marketing authorisation granted in Member State A; and

(d) the marketing authorisations referred to in (a) and (c) above were granted to different members of the same group of companies and the manufacturers of medicinal products X and Y are also members of that group of companies; and

(e) companies within the same group as the holder of the marketing authorisation for product X continue to manufacture and market product X in Member States other than Member State B?

2. To what extent is it relevant to the answer to Question 1 that:

(a) the marketing authorisation for medicinal product X ceased to have effect in Member State B as a result of voluntary surrender on the part of the person to whom it had been granted; and/or

(b) the formulation of medicinal product Y was developed and introduced in order to provide a benefit to public health which medicinal product X (manufactured according to a different formulation) does not provide; and/or

(c) that benefit to public health would not be achieved if product X and product Y are both on the market in Member State B at the same time; and/or

(d) the differences between the formulations of medicinal product X and medicinal product Y are such that neither product may lawfully be marketed under the marketing authorisation applicable to the other; and/or

(e) the competent authority possesses the relevant data required under Directive 65/65 in relation to both product X and product Y; and/or

(f) the competent authority considers that the prohibition on imports of product X from Member State A would have the effect of partitioning the market; and/or

(g) the competent authority considers that there are no grounds within

Article 36 of the EC Treaty which would justify a prohibition on imports and sales of product X?‘

**The questions referred for a preliminary ruling**

22. In order to answer the questions referred for a preliminary ruling, which may be examined together, it is necessary to ascertain whether imports of the old version of Zimovane may in fact be treated as parallel imports, in which case the normal procedure under the Directive relating to the issue of marketing authorisations does not apply.

23. The first point to note is that notwithstanding the Treaty rules on the free movement of goods no medicinal product may be placed on the market in a Member State unless a marketing authorisation has been issued in accordance with the Directive by the competent authority of that State. An application for a marketing authorisation for a medicinal product submitted by the person responsible for placing it on the market must contain the information and be accompanied by the documents listed in Article 4 of the Directive even where the medicinal product concerned is already the subject of an authorisation issued by the competent authority of another Member State.

24. However, those principles are subject to exceptions arising, on the one hand, from the Directive itself and, on the other, from the Treaty rules relating to the free movement of goods.

25. Accordingly, point 8 of Article 4 of Directive 65/65/EEC, as amended by Council Directive 87/21/EEC of 22 December 1986 (OJ 1987 L 15, p. 36), establishes an 'abridged‘ procedure which, subject to certain conditions, relieves the manufacturers of medicinal products which are essentially similar to medicinal products already authorised from having to provide the results of pharmacological and toxicological tests and of clinical trials, thus saving the time and expense necessary to assemble such data, and avoiding the repetition of tests on humans or animals where these are not absolutely necessary (see **Case C-368/96 Generics (UK) and Others [1998] ECR I-7967, paragraphs 2 to 4**).

26. The other exception, which is relevant in this case, is defined in De Peijper. In that case, the Court held, at paragraphs 21 and 36, in the context of Articles 30 and 36 of the Treaty, that if, as a result of importation on a previous occasion which gave rise to the grant, by them, of a marketing authorisation, the public health authorities of the Member State of importation are already in possession of all the particulars necessary for checking that the product is effective and safe, it is not necessary, for the purpose of protecting the health and life of humans, for those authorities to require a second trader who has imported a medicinal product which is in every respect the same or which has no differences altering the therapeutic effect, to submit the abovementioned particulars to them again.

27. In Case C-201/94 Smith & Nephew and Primecrown [1996] ECR I-5819, paragraph 21, the Court stated again that the Directive cannot apply to a medicinal product covered by a marketing authorisation in one Member State which is being imported into another Member State as a parallel import of a product already covered by a marketing authorisation in that other Member State, because the imported medicinal product cannot, in such a case, be regarded as being placed on the market for the first time in the Member State of importation.

28. The Court went on to state, in paragraphs 25 and 26 of that judgment, that in order to ascertain whether imports of a medicinal product constitute parallel imports the competent authority in the Member State of importation must verify that the two medicinal products have a common origin and, if not identical in all respects, have at least been manufactured according to the same formulation, using the same active ingredient, and have the same therapeutic effect.

29. In the light of that case-law, it is important to note that in the present case it is common ground that the medicinal products at issue in the main proceedings contain the same active ingredients and have the same

therapeutic effect and a common origin, since they come from manufacturers belonging to the same group of companies.

30. However, it is clear from the observations submitted to the Court that there are other particular circumstances of the case which might cast doubt on the compliance with Community law of the decisions of the United Kingdom authorities at issue.

31. M & B and RPR claim that the provisions of Community law relating to the parallel importation of medicinal products apply only for so long as the product concerned is covered by marketing authorisations which are simultaneously in force in the Member State of exportation and the Member State of importation. In this case, it would therefore have been unlawful to apply the procedure set out in MAL

(PI) with a view to authorising imports into the United Kingdom of the old version of Zimovane. First, the parent authorisation of the old version of the medicinal product was revoked and, second, the condition established by the Court in Smith & Nephew and Primecrown of 'manufacture according to the same formulation‘ was not met. According to M & B and RPR, this latter condition includes both active ingredients and excipients. They add that their decision to distribute only the new version of Zimovane in the United Kingdom and to surrender the authorisations relating to the old version is explained by the need to achieve, primarily in that Member State, a particular benefit for public health — a benefit which could not be achieved if the old and new versions of the product were both available on the United Kingdom market at the same time.

32. The French Government observes that, even if the excipient is not relevant to the therapeutic effect, it is considered to be a part of the qualitative and quantitative particulars of the product as referred to in the Directive, since it is part of the formulation of the product. Therefore, unless a new marketing authorisation is obtained in accordance with the provisions of the Directive, imports of the old version of Zimovane cannot be treated as parallel imports within the meaning of the case-law of the Court.

33. The Commission observes that, according to Articles 3 and 4 of the Directive, marketing authorisations are given for a specific medicinal product, which has been evaluated by means of a stringent authorisation procedure, taking into account the product as a whole, including the excipients. The composition of a medicinal product includes both the active ingredients and the excipients. All the constituents of a medicinal product are of importance to the quality, efficacy and safety of the product and form part of the summary of product characteristics of a medicinal product required by Article 4a of the Directive. That summary is an integral part of the authorisation for any medicinal product. In this case, the differences between the old and new versions are therefore not without importance. The Commission adds that, if the marketing authorisation for a medicinal product is revoked, there is no obligation to submit information regularly in connection with renewal of the authorisation, in accordance with the pharmacovigilance system established by Directive 75/319. As a result, the competent authorities in the State of importation cannot be sure that the use of the old product imported in parallel is still safe, according to the latest scientific data.

34. According to the United Kingdom Government, in circumstances such as those of this case, the MCA is required, under Article 30 of the Treaty, to allow parallel imports of the old version of Zimovane onto the United Kingdom market. There is no reason to treat the two versions of the product as different medicinal products. That would require parallel importers of the old version of Zimovane to obtain a marketing authorisation within the meaning of the Directive, if indeed that were actually possible (given the insuperable difficulty of repeating the chemical, pharmaceutical and biological tests required by the Directive). The old and new products are, from the therapeutic point of view, in normal conditions of use, equivalent versions of a product with a common origin and the same active ingredient. Changes in the excipients of a medicinal product do not, in general, alter the therapeutic effect.

35. Whilst acknowledging that RPR did not consciously attempt to isolate the United Kingdom market from the rest of the Community market, the United Kingdom Government observes that, if RPR's arguments were accepted, the voluntary surrender of the marketing authorisation for the old version of Zimovane would have precisely the effect of thus partitioning the market. Notwithstanding the formal revocation of the parent authorisation, the MCA is in possession of all the data, documents and details required by Article 4 of the Directive for the purpose of monitoring the efficacy and safety of the medicinal product which is to be the subject of a parallel importation. It is also in a position, in the future, by virtue of the rules that exist in relation to pharmacovigilance, to acquire the information needed to be sure that the old version of Zimovane does not pose a problem for public health, so long as there are marketing authorisations in other Member States.

36. The United Kingdom Government observes, finally, that the general interest in safeguarding public health, even if it were understood in the sense relied upon by M & B and RPR, does not require a measure such as a complete ban on parallel imports of the old version of the product.

37. The Swedish Government submits that the two versions of Zimovane are sufficiently alike for them to be treated as the same product. If the obligation for the formulation to be identical were to be understood as meaning the whole formulation of the medicinal products, this would create unjustified obstacles to intra-Community trade.

38. It appears, therefore, that the criticism of the contested decisions of the United Kingdom authorities is based, in particular, on the fact that those decisions could be contrary to Community law for the following three reasons:

— the two versions of Zimovane are not manufactured according to the same formulation, the new version being manufactured using different excipients and by a different manufacturing process;
— the pharmacovigilance system will not work because after the parent marketing authorisation is revoked the holder of the marketing authorisation is no longer obliged to submit information regularly in relation to the old version of the medicinal product; and
— the particular benefit for public health which is provided by the new version of Zimovane as compared with the old version could not be achieved if the
old and new versions of the medicinal product were both available on theUnited Kingdom market at the same time.
39. Before examining each of those three grounds for criticising the parallel import licences at issue, it is important to note that it is not necessary to rule on the question of lawfulness in the light of the free movement of goods of the automatic revocation of parallel import licences as a result of the revocation of a parent authorisation at the request of the holder of that authorisation. That question does not arise in this case because the United Kingdom authorities have acknowledged that the parallel import licences for the old version of Zimovane are appended to the marketing authorisation issued for the new version.
40. Next, it should be noted that although, as the Court held in De Peijper and Smith & Nephew and Primecrown, it follows from Articles 30 and 36 of the Treaty that national authorities must not obstruct parallel imports by requiring parallel importers to satisfy the same requirements as those which are applicable to undertakings applying for the first time for a marketing authorisation for a medicinal product, that principle is subject to the condition that an exception of that kind to the rules normally applicable to marketing authorisations for medicinal products does not undermine the protection of public health. As is clear from the first recital in the preamble to the Directive, the primary purpose of any rules concerning the production and distribution of medicinal products must be to safeguard public health. The criteria which must be met by a product imported as a parallel import for the parallel importer to be under no obligation to supply the particulars referred to in the Directive must not, therefore, lead to a relaxation of safety requirements (see, to that effect, Generics (UK), paragraph 22).
41. It must also be borne in mind that there would be a real obstacle to intra-Community trade if importers of the old version of Zimovane, which is still authorised in other Member States and lawfully marketed there, were not able to use the simplified procedure open to parallel importers in accordance with MAL 2 (PI).
42. As is clear from paragraph 35 of this judgment, the competent authorities in the United Kingdom considered it possible to authorise the placing on the market of those medicinal products imported as parallel imports by using as a parent marketing authorisation the authorisation for the new version of Zimovane and they have taken the view that, on the basis of the information in their possession, in spite of the different excipients used, the old version of Zimovane clearly remained effective and safe.
43. Although, as the United Kingdom Government has submitted, differences in the excipients used in medicinal products do not normally have any effect on safety, it is not disputed that such effects can exist. It is possible for a medicinal product imported as a parallel import, which contains the same active ingredients and has the same therapeutic effect but does not use the same excipients as the medicinal
oduct which is the subject of the marketing authorisation in the Member State of importation, to show significant differences from the authorised product in terms of safety, given that modifications to the formulation of a medicinal product in respect of the excipients may have an effect on the shelf-life and the bioavailability of the product, for example in relation to the rates at which the medicinal product dissolves or is absorbed (see also, to that effect, Generics (UK), paragraph 32).
44. However, the possibility of such effects on safety does not mean that as a consequence of differences relating to the excipients used the national authorities may never resort to simplified procedures for the licences granted to parallel importers.
45. The national authorities are required to authorise, in accordance with the rules relating to parallel imports, a medicinal product imported as a parallel product where they are convinced that that product, in spite of differences relating to the excipients, does not pose a problem for public health. Accordingly, the competent authorities of the Member State of importation must ensure, at the time of import and on the basis of information in their possession, that the medicinal product imported as a parallel product, even if not identical in all respects to that already authorised by them, has the same active ingredient and the same therapeutic effect and does not pose a problem of quality, efficacy or safety (see, to that effect, Case C-100/96 British Agrochemicals Association [1999] ECR I-1499, paragraph 40).
46. As regards the problem raised in relation to pharmacovigilance, it is sufficient that pharmacovigilance satisfying the relevant requirements of Directive 75/319 as amended can be ensured for medicinal products imported as parallel imports, like those in this case, through cooperation with the national authorities of the other Member States by means of access to the documents and data, produced by the manufacturer or other companies in the same group, relating to the old version in the Member States in which that version is still marketed on the basis of a marketing authorisation still in force. In addition, it is possible to compel the holder of the marketing authorisation in the Member State of importation, who belongs to the group of companies which is in possession of the marketing authorisations for the old version in the other Member States, to supply the necessary information (see, to that effect, De Peijper, paragraphs 26 and 27).

47. Finally, it is necessary to examine the argument put forward by M & B and RPR that the particular benefit to public health provided by the new version of Zimovane as compared with the old version would not be achieved if the old version of Zimovane were present on the United Kingdom market. In that regard, it is sufficient to state that, even if the argument were well founded, it does not follow that, in circumstances such as those of the main case, the national authorities are compelled to require parallel importers to follow the procedure laid down in the Directive if they take the view that, in normal conditions of use, as referred to in Article 5 of the Directive, the medicinal product imported as a parallel import does not pose a risk as to quality, efficacy or safety.

48. In the light of the foregoing, the answer to the questions referred for a preliminary ruling must be that where it is sought to import medicinal product X from Member State A into Member State B, it is permissible for the person who proposes to place the imported product upon the market in Member State B to seek and obtain a parallel import licence from the competent authority in Member State B without complying with all the requirements of the Directive if:

— medicinal product X is the subject of a marketing authorisation granted in Member State A and was the subject of a marketing authorisation which has ceased to have effect in Member State B;

— medicinal product Y is the subject of a marketing authorisation granted in Member State B, but is not the subject of a marketing authorisation granted in Member State A;

— medicinal product X has the same active ingredients and therapeutic effect as medicinal product Y, but does not use the same excipients and is manufactured by a different manufacturing process, where the competent authority in Member State B is in a position to verify that medicinal product X complies with the requirements relating to quality, efficacy and safety in normal conditions of use and is in a position to ensure normal pharmacovigilance;

— the marketing authorisations referred to above were granted to different members of the same group of companies and the manufacturers of medicinal products X and Y are also members of that group of companies; and

— companies within the same group as the holder of the marketing authorisation for product X which has been withdrawn in Member State B continue to manufacture and market product X in Member States other than Member State B.

In such a situation, the competent authority is not required to take into consideration the fact that medicinal product Y was developed and introduced in order to provide a particular benefit to public health which medicinal product X does not provide and/or that that particular benefit to public health would not be achieved if product X and product Y were both on the market in Member State B at the same time.

**Costs**

49. The costs incurred by the United Kingdom, French and Swedish Governments and by the Commission, which have submitted observations to the Court, are not recoverable. Since these proceedings are, for the parties to the main proceedings, a step in the proceedings pending before the national court, the decision on costs is a matter for that court.

On those grounds,

THE COURT,

in answer to the questions referred to it by the High Court of Justice of England & Wales, Queen's Bench Division, by order of 31 July 1997, hereby rules:

Where it is sought to import medicinal product X from Member State A into Member State B, it is permissible for the person who proposes to place the imported product upon the market in Member State B to seek and obtain a parallel import licence from the competent authority in Member State B without complying with all the requirements of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products (OJ, English Special Edition 1965-1966, p. 20), as amended by Council Directive 93/39/EEC of 14 June 1993, if:

— medicinal product X is the subject of a marketing authorisation granted in Member State A and was the subject of a marketing authorisation which has ceased to have effect in Member State B;

— medicinal product Y is the subject of a marketing authorisation granted in Member State B, but is not the subject of a marketing authorisation granted in Member State A;

— medicinal product X has the same active ingredients and therapeutic effect as medicinal product Y, but does not use the same excipients and is manufactured by a different manufacturing process, where the competent authority in Member State B is in a position to verify that medicinal product X complies with the requirements relating to quality, efficacy and safety in normal conditions of use and is in a position to ensure normal pharmacovigilance;

— the marketing authorisations referred to above were granted to different members of the same group of companies and the manufacturers of medicinal products X and Y are also members of that group of companies; and

— companies within the same group as the holder of the marketing authorisation for product X which has been withdrawn in Member State B continue to manufacture and market product X in Member States other than Member State B.

In such a situation, the competent authority is not required to take into consideration the fact that medicinal product Y was developed and introduced in order to provide a particular benefit to public health which medicinal product X does not provide and/or that that particular benefit to public health would not be achieved if product X and product Y were both on the market in Member State B at the same time.

**OPINION OF ADVOCATE GENERAL LA PERGOLA**

delivered on 19 May 1999 (1)
Provisional text
Case C-94/98
The Queen
v
The Licensing Authority established by the Medicines Act 1968
(acting by the Medicines Control Agency)
ex parte: Rhône-Poulenc Rorer Limited and May & Baker Limited
(Request for a preliminary ruling from the High Court of Justice, Queen's Bench Division)
(Medicinal preparations — Marketing authorisation — Parallel imports)

**I — The factual and legislative context of the main proceedings and the questions referred**

1. By an order received at the Court Registry on 2 April 1998, the High Court of Justice, Queen's Bench Division, submitted two questions, concerning the interpretation of (i) Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, as repeatedly amended on the basis of the experience acquired after its adoption and in order to bring it into line with scientific progress ('the Directive') (2) and (ii) of the provisions of the Treaty concerning the free movement of goods.

2. By means of the Directive, based on Article 94 EC (ex-Article 100) (3) the Community legislature sought to remove obstacles to trade in medicinal products and to the development of the pharmaceutical industry in the internal market deriving from differences in the legislation of the Member States regarding the production and distribution of such products. The method chosen to achieve free movement of medicinal products was progressive approximation of national laws, the primary purpose of which was expressly stated to be 'to safeguard public
alth'. (4) In particular, the Directive extensively harmonised the rules on quality, safety and efficacy which must be observed by the authorities responsible for issuing marketing authorisations for medicinal products.

3. No medicinal product may be offered for sale in a Member State without a marketing authorisation ('MA') having first been issued in respect of it by the competent authorities of that State in accordance with the Directive (see the first paragraph of Article 3 of the Directive). (5) An application for an MA for a medicinal product, lodged by the person responsible for placing the product on the market, must contain the information and be accompanied by the documents particularised in Article 4 of the Directive, even if the medicinal product in question is already the subject of an MA issued by the competent authority in another Member State. (6) According to the annex to Directive 75/318/EEC, (7) the particulars and documents accompanying an application for an MA submitted in accordance with Article 4 comprise the following parts: (i) a summary of the dossier, (ii) chemical, pharmaceutical and biological tests of the medicinal products, (iii) toxicological and pharmacological tests, and (iv) clinical documentation. The application must contain all the information necessary to assess the product in question, including any unfavourable information. Moreover, in order to monitor the positive and negative effects after issue of the MA, the holder must notify the competent authorities of all changes in data, new information not contained in the initial application and pharmacovigilance reports (see below, footnote 25 and relevant part of text).

4. The competent authority may refuse to grant an MA only if, after examining the application, it determines that: (a) the information and documents supplied by the applicant are irregular or incomplete, (b) the product is harmful under normal conditions of use, (c) its therapeutic efficacy is lacking or has not been sufficiently substantiated by the applicant, or (d) the qualitative and quantitative composition of the product is not as declared (see Articles 5 and 21 of the Directive). An MA, which is valid for five years, may be renewed for like periods on application by the holder at least three months before expiry (Article 10, first paragraph). As Article 9 of the Directive states, the grant of an MA does not affect the civil and criminal liability of the manufacturer and, where applicable, of the person responsible for placing the product on the market.

5. Article 11 (in conjunction with Article 21) of the Directive goes on to say that an MA may be suspended or revoked on the following grounds only: (a) the product proves to be harmful in normal conditions of use or (b) its therapeutic efficacy is lacking or (c) its qualitative and quantitative composition is not as declared by the applicant, (d) the information in the file is incorrect or has not been amended in accordance with Article 9a (concerning changes to methods of preparation and control to bring them into line with scientific and technical progress) or (e) checks have not been carried out on the ingredients, intermediate products and finished products in accordance with the methods described by the applicant.

As outlined in greater detail below (see point 10), the present case is concerned with a measure ordering the revocation of an MA for a medicinal product. This case, however, displays the peculiar feature that the revocation was ordered by the competent national authority in response to a request from the holder of the MA, purporting to be based on pressing reasons of protection of public health. More specifically, the issue in the main proceedings is whether and to what extent revocation of the original MA may affect the freedom of economic operators outside the official distribution channels of the holder of the MA to carry out parallel imports of a different variant of the product from other Member States where it is sold at lower prices than those charged in the importing country.

6. As this Court held in De Peijper, the freedom to undertake parallel imports of products properly placed on the market is recognised in Community law, notwith-

standing the operation in the Member States of MA systems whose effects are limited to national territory. According to the Court, the fact that parallel importers quite often offer the goods at a price lower than that charged by the duly appointed importer 'should ... encourage the public health authorities not to place parallel imports at a disadvantage, since the effective protection of health and life of humans also demands that medicinal preparations should be sold at reasonable prices'. (8) According to that judgment, it must be borne in mind that, in the sphere

free movement of medicinal products, the requirement of protecting public health has two aspects. First, it may justify application to the national MA systems, involving State measures equivalent to quantitative restrictions on imports, of the derogation provided for in Article 36 of the EC Treaty (which now, after amendment, Article 30 EC) (9) from the prohibition of imposing such measures laid down in Article 30 of the EC Treaty (now, after amendment, Article 28 EC). Secondly, where it is necessary to verify whether the requirements for that derogation are fulfilled, including the requirement that any harm done by the national measure restricting intra-Community trade is the minimum called for by the general interest in protecting human health, it must be borne in mind that that interest can be effectively pursued by the Member States precisely by safeguarding the freedom of economic operators to compete vigorously on prices thanks to parallel imports.

7. In De Peijper, the Rotterdam Kantonrechter (district public prosecutor) had commenced criminal proceedings for infringement of Netherlands health legislation against an unauthorised importer of certain medicinal products, who was operating without having in his possession the file (concerning the medicinal product in the abstract) and the so-called 'records' (relating to checks of individual batches of imported goods) for the products in question. The accused, a director of a company which had acquired the medicinal products from a British wholesaler, contended in his defence that he had not been able to obtain the documents prescribed by the Netherlands legislation either from the manufacturer or from the latter's exclusive concessionaire in the Netherlands. (10) In answer to the two

questions on which the Kantonrechter, Rotterdam, sought a preliminary ruling, (11) the Court held, first of all, that Article 30 of the EC Treaty (now, after amendment, Article 28 EC) precludes national legislation or practice which results in the channelling of imports in favour of only certain economic operators. The Court then interpreted Article 36 of the Treaty (now, after amendment, Article 30 EC) to the effect that it 'cannot be relied on to justify [national] rules or practices which, even though they are beneficial, contain restrictions which are explained primarily by a concern to lighten the administration's burden or reduce public expenditure, unless, in the absence of the said rules or practices, this burden or expenditure clearly would exceed the limits of what can reasonably be required'. (12) In the circumstances described in the first question from the Netherlands Court (see footnote 10), the Court said, the principle of proportionality was infringed by legislation or practice which made the grant of an MA for medicinal products subject to the condition that the parallel importer must supply to the competent authority in the Member State of importation documents identical to those already lodged by the manufacturer or its exclusive concessionaire; in such circumstances, the latter would be allowed to monopolise imports and marketing of the medicinal product in question by refusing to produce documents relating to the product in general or to a particular batch. A national measure like the one at issue could, on the other hand, qualify for the derogation provided for in Article 36 of the EC Treaty (now, after amendment, Article 30 EC) where it was clear that any other measure would impose a clearly greater than normal burden on the national administration. (13) Finally, as is apparent from paragraph 3 of the operative part of the judgment in De Peijper, the principles mentioned there apply to each of the procedures for authorisation which theoretically become necessary where it is clear from the documents deposited by the manufacturer or its exclusive representative in support of the application for the MA that: (i) that several variants of a uniform medicinal product are produced and marketed under the same name in more than one Member State and that (ii) the differences between the variants, regarding the manufacturing process or the qualitative and quantitative composition of the product in question, have an impact on its therapeutic effect. Only in such circumstances, according to the Court, would there be 'any justification for treating the variants as different medicinal preparations, for the purpose of authorising them to be placed on the market and as regards producing the relevant documents'. (14)

8. Following the judgment in De Peijper, the Commission considered it appropriate to submit to the Council a proposal for a directive on parallel imports of proprietary medicinal preparations. (15) However, considering approval of the document by the Council to be 'improbable', in particular following objections from the Economic and Social Committee and the vote against it of 16 October 1981 by the European Parliament, the Commission subsequently decided to withdraw that proposal. The principles inspiring the document were nevertheless

blished in the form of guidelines for Member States and the relevant economic operators. (16) I think it is relevant to consider that Commission initiative at this stage because, as is stated in the order for reference, great inspiration was drawn from that communication in 1984 by the Medicines Control Agency ('MCA') — that is to say, the executive agency vested with the regulatory powers of the Licensing Authority set up by the Medicines Act 1968 — when it in turn adopted guidelines concerning the procedures to be observed when applying for MAs for parallel imports of medicinal preparations into the United Kingdom. (17)

9. MAL 2 (PI) defines 'parallel imports' as meeting two requirements: the product is the subject of an MA

in the United Kingdom and the applicant seeks to import from another Member State a version of that product which already has an MA issued by another Member State. In such cases, the MCA follows a simplified procedure, which is generally more expeditious than that provided for by the Directive, under which the applicant for an MA for parallel imports of medicinal products (known as the Product Licence (Parallel Import), hereinafter 'PL (PI)‘) is required to provide less extensive information than is required for an application in accordance with the Directive. To qualify for that procedure, the medicinal product must satisfy several conditions, in particular it must have been made by or under licence to the manufacturer who made the product covered by the United Kingdom MA or a member of the same group of companies. (18)

10. This Court delivered another important judgment concerning parallel imports of medicinal products in 1996, a little more than 20 years after De Peijper. The High Court of Justice (the court from which today's questions emanate) had asked the Court of Justice to provide the requisite guidance for interpretation of the Directive, and of the obligations associated with MAs for medicinal preparations, in order to determine disputes between Smith & Nephew Pharmaceuticals ('S&N‘) and the MCA and the competing company Primecrown, and secondly, between Primecrown and the MCA. (19) Those disputes arose from the grant in August 1993 of a PL(PI) to Primecrown for a medicinal product manufactured in Belgium, where it was covered by an MA. The product of Belgian origin had the same name and was manufactured under a licensing agreement concluded with the same licensor for a product for which S&N had held a United Kingdom MA since January 1991. (20) Because the PL(PI) had been granted to Primecrown on the false assumption that there existed between S&N and Marion Merrel Dow Belgium the corporate link required for application of the simplifiedprocedure (see above, footnote 17 and relevant part of the text), the licence was subsequently annulled by the MCA after it discovered the error. The Court held, first, that the obligation of an applicant for an MA to produce the necessary information and documents prescribed by the Directive in order to verify that a medicinal product is effective and harmless is justified only for medicinal products which are being put on the market for the first time. That obligation cannot, however, be relied on by the competent authority of a Member State in order to protect public health in relation to a medicinal product already covered by an MA in another Member State and of which the import into the first country constitutes a parallel import of a product already covered by another MA. (21) According to the Court, therefore, in a case such as this one — in which the medicinal product manufactured in the importing State and the one brought in as a parallel import, even though manufactured under licence by independent companies, ultimately originated from the same licensor — the rule in De Peijper should apply (see point 7 above) otherwise such agreements could lead to partitioning of the national markets of the various Member States. (22) That case-law, said the Court in paragraph 26 of the judgment, is applicable not only where the proprietary medicinal product covered by an original MA in the importing State and the one brought in as a parallel import are identical in all respects, but also where the two medicinal products 'have at least been manufactured according to the same formulation, using the same active ingredients and ... have the same therapeutic effects‘. Consequently, the Court concluded that the competent authority of a Member State — if it concludes that a medicinal product covered by an MA in another Member State and a medicinal product for which it has already issued an MA, manufactured by independent companies under agreements with the same licensor, although not identical in every respect, are at least manufactured in accordance with the same formulation and using the same active ingredients and having the same therapeutic effects — must extend the benefit of that MA to the imported product. That obligation becomes inoperative only if there are reasons relating to effective protection of human life and health. Where, on the other hand, the competent national authority reaches the conclusion that the medicinal product intended to be imported on a parallel basis does not satisfy the criteria mentioned here — and cannot, therefore, be regarded as already on the market in the importing Member State — a new MA will become necessary, which may be granted only in accordance with the conditions laid down in Articles 3 and 4 of the Directive. (23)

11. That is the context, in terms of legislation and case-law, of the questions referred in this case. I shall now consider the facts giving rise to the main proceedings, as described by the national court. In 1989 and 1993 the MCA granted May & Baker ('M&B‘) a total of five marketing authorisations for the United Kingdom (24) for zopiclone, a hypnotic used for the short-term treatment of insomnia, marketed in most of the Member States under the brand name Imovane and in the United Kingdom the name Zimovane. Under an agreement concluded in 1992, M&B appointed Rhône-Poulenc Rorer (the two companies being hereinafter jointly referred to as 'RPR‘) as its agent for the production and distribution of certain medicinal products, including Zimovane. In 1996 RPR

proved, following research and development for more than three years, costing around UKL 1 500 000, a new version of Zimovane which is particularly beneficial for public health, described in the confidential annex to the order for reference ('the confidential annex‘). The 'new Zimovane‘ contains the same active ingredient and has the same therapeutic effect as the 'old Zimovane‘ but is prepared by a different production process using different excipients (an excipient is a inert substance used as a diluent or vehicle for a pharmaceutical product). In order to place the new version of the product on the market in the United Kingdom, in July 1996 RPR, after providing the information and documents prescribed by the Directive, obtained variations to two authorisations (numbers 0012/0259 and 0012/0260) which had not yet been

used. At the request of RPR, the MCA also revoked MA number 0012/0162 on the basis of which the old version of Zimovane had been distributed in the United Kingdom, and of (unused) authorisations numbers 0012/0163 and 0012/0164. Thus, as from 1 August 1996, RPR ceased to market, directly or under licence, the old version of Zimovane in the United Kingdom and distributes only the new version, in the form of 3.75 mg or 7.5 mg tablets. The old version of Zimovane nevertheless continues to be distributed in the other Member States (with the exception of Portugal). However, it is RPR's intention to replace the old version by the new version of the medicinal product, as it had done in the United Kingdom, in step with the issue of marketing authorisations by the competent authorities in the Member States. (25) RPR considers that it would be committing a criminal offence if it distributed the new version of Zimovane on the basis of authorisations for the old version or if it marketed the old version of Zimovane on the basis of the MA for the new product.

12. In accordance with paragraph 12 of MAL 2 (PI) (see footnote 17 above), seven authorisations for parallel imports of the old version of Zimovane into the United Kingdom, which had previously been granted to five operators, became invalid as from 31 July 1996 as a result of revocation of the 'mother‘ authorisation, directed by the MCA at the request of RPR (see point 11 above). Upon being notified by the MCA (in accordance with paragraph 21 of MAL 2 (PI)), the holders of the authorisations in question therefore applied for the variations needed to 'anchor‘ them to a valid reference MA, specifically MA number 0012/0259. The MCA decision to grant or maintain in force, under the abridged procedure, the seven authorisations for the old version of Zimovane (in 7.5 mg tablets) is one of the two measures challenged by RPR in the main proceedings. The second measure contested by RPR is the MCA's decision to grant to each of three other operators, again under the MAL 2 (PI) procedure, an authorisation for parallel imports of the old version of Zimovane (in 7.5 mg tablets) into the United Kingdom from Spain.

13. According to the High Court of Justice, a preliminary ruling is needed on the following questions in order to give judgment in the main proceedings:

'1. In a case where medicinal product X is sought to be imported from Member State A into Member State B, is it permissible for the person who proposes to place the imported product upon the market in Member State B to seek and obtain a marketing authorisation from the competent authority in Member State B without complying with the requirements of the Council Directive 65/65/EEC (as amended) if:

(i) medicinal product X is the subject of a marketing authorisation granted in Member State A and was the subject of a marketing authorisation which has ceased to have effect in Member State B; and

(ii) medicinal product X has the same active ingredients and therapeutic effect as medicinal product Y, but is not manufactured according to the same formulation as medicinal product Y; and

(iii) medicinal product Y is the subject of a marketing authorisation granted in Member State B, but is not the subject of a marketing authorisation granted in Member State A; and

(iv) the marketing authorisations referred to in (i) and (iii) above were granted to different members of the same group of companies and the manufacturers of medicinal products X and Y are also members of that group of companies; and

(v) companies within the same group as the holder of the marketing authorisation for product X continue to manufacture and market product X in Member States other than Member State B?

2. To what extent is it relevant to the answer to Question 1 that:

(i) the marketing authorisation for medicinal product X ceased to have effect in Member State B as a result of voluntary surrender on the part of the person to whom it had been granted; and/or

(ii) the formulation of medicinal product Y was developed and introduced in order to provide a benefit to public health which medicinal product X (manufactured according to a different formulation) does not provide; and/or

(iii) that benefit to public health would not be achieved if product X and product Y are both on the market in Member State B at the same time; and/or

(iv) the differences between the formulations of medicinal product X and medicinal product Y are such that neither product may lawfully be marketed under the marketing authorisation applicable to the other; and/or

(v) the competent authority possesses the relevant data required under Directive 65/65 in relation to both product X and product Y; and/or

(vi) the competent authority considers that the prohibition on imports of product X from Member State A would have the effect of partitioning the market; and/or

(vii) the competent authority considers that there are no grounds within Article 36 of the EC Treaty [now, after amendment, Article 30 EC] which would justify a prohibition on imports and sales of product X?‘

**II — The submissions of the parties to the main proceedings and the observations of the Member States and the Commission**

14. RPR states that the Community provisions on parallel imports of medicinal products apply only if the product in question is covered by valid authorisations in both the exporting and importing Member States. According to RPR, recourse to the MAL 2 (PI) procedure for the purpose of authorising imports into the United Kingdom of the old version of Zimovane after 31 July 1996 was unlawful. First, the 'mother‘ MA for the old version of the product was revoked and, second, the requirement of 'manufacture according to the same formulation‘ was likewise not satisfied, that criterion having been established by the Court in Smith &

Nephew, with the result that an imported medicinal product may not qualify for the simplified procedure on the basis of an original MA issued for a similar product by the competent authority in the importing Member State. RPR maintains that the old and new versions of Zimovane are not manufactured in accordance with the same formulation. That term should in its view be construed as a synonym of 'recipe‘ and includes both the active ingredients and the excipient. Therefore, the MCA should have required the parallel importers to produce a complete dossier, in accordance with the procedure provided for and governed by the Directive.

15. RPR adds that its decision to distribute only the new version of Zimovane in the United Kingdom and surrender the marketing authorisations for the old version had neither the object nor the effect of artificially partitioning the domestic market. Precedence was given to introduction of the new version of Zimovane in the United Kingdom because it was necessary to achieve first of all in that Member State the public health benefit described in the confidential annex. That benefit could not, however, be achieved if both the old and the new versions of the product had been available on the British market.

16. According to the United Kingdom, in the circumstances of this case the MCA is required, pursuant to Article 30 of the EC Treaty (now, after amendment, Article 28 EC), to allow parallel imports of the old version of Zimovane into the United Kingdom market to continue. There is no reason to regard the two versions as different medicinal products, with the result that it would be necessary for the parallel importers of the old version of Zimovane to obtain an MA under the Directive, if indeed that were actually possible (regard being had to the unsurmountable difficulties presented by the chemical, pharmaceutical and biological tests prescribed by the Directive). The old and the new medicinal products, manufactured by the same group of companies, are from the therapeutical point of view, under normal conditions of use, equivalent versions of a product having a common origin and the same active ingredient (zopiclone). A change to the excipients in a medicinal product is in general neutral as regards its therapeutic effect. Although conceding that the plaintiffs have not consciously sought to isolate the United Kingdom market from the remainder of the Community, the United Kingdom authorities submit that voluntary withdrawal of the MA for the old version of Zimovane would result in such fragmentation, if RPR‘s arguments were to be upheld.

17. The United Kingdom submits, finally, that the general interest in the protection of public health, even if construed in the manner contended for by RPR and described in the confidential annex, does not call for a drastic measure such as the total blocking of parallel imports of the old version of the product. Notwithstanding the formal revocation of the 'mother‘ authorisation, the MCA still has at its disposal all the data, documents and details prescribed by Article 4 of the Directive to monitor the efficacy and harmlessness of the medicinal product intended to be the subject of parallel imports. The MCA states that it received them from RPR in connection with the procedure for the issue of an MA for the new version of the product in question, which contains the same active ingredients and has the same therapeutic effects.

18. France and the Commission have submitted to the Court arguments substantially similar to those of RPR. The Commission maintains in particular that the claim that the MCA had relevant information at its disposal for both variants of Zimovane (see point 17 above), although true when the MAs for the old version were surrendered, has ceased to be true with the passage of time. As from 1 August 1996 RPR is no longer required to submit to the MCA, periodically or when applying for renewal of an MA, the information concerning the old version of Zimovane required by the provisions on pharmacovigilance (see Article 29d of Directive 79/319/EEC and Article 10 of Directive 65/65/EEC). (26) Those obligations moreover do not apply to parallel importers either, regardless of whether those economic operators actually possess the relevant data. The Commission therefore submits that the MCA is no longer in a position to assess the safety of the version of the medicinal product imported into the United Kingdom on the basis of the most up-to-date scientific data. The United Kingdomauthorities contend that compliance with the pharmaceutical monitoring requirements mentioned by the Commission could be ensured (i) by virtue of RPR's obligation to provide up-to-date information regarding the new version of Zimovane or (ii) even if it were conceded that the two variants of the medicinal product constituted different products, by means of cooperation with the other national authorities in accordance with the criterion laid down by the Court in paragraph 27 of the De Peijper judgment, through access to the documents and data produced by RPR or other companies in its group for the old version in the Member States in which it is still being marketed on the basis of a valid marketing authorisation.

**III — Legal Analysis**

19. This case, in my opinion, displays an important and unusual feature which distinguishes it both from the two earlier ones already referred to several times and from almost all the cases in which the Court is called on to interpret the Treaty provisions on the free movement of goods. In this case a State administration is arguing that a particular measure invoked by an economic operator is, in the circumstances of the case, contrary to Article 30 in that it unduly restricts parallel imports. That measure is the decision requiring an application to be submitted in accordance with the Directive as a precondition for the issue of an authorisation to effect parallel imports of a medicinal product for which no 'mother‘ MA exists any longer in the importing Member State. The other party contends, for its part, that the adoption of the measure in question is required in order to protect public health, on the basis of Article 36 of the EC Treaty (now, after amendment, Article 30 EC). In addition, the analysis of today's preliminary questions cannot overlook the specific nature

of medicinal products, (27) by reason of which, as I have several times observed, the freedom of movement guaranteed by the Treaty does not apply unconditionally to those goods. Indeed, as is clear from the case-law of the Court, 'Member States are entitled, at the present stage of harmonisation and in the absence of a procedure for Community authorisation or mutual recognition of national authorisations, to prohibit entirely the marketing of medicinal products which have not been authorised by the competent national authorities' (28) (29) The Court's explanation for that finding was that it is the responsibility of the Member States, within the limits imposed by the Treaty, to decide what level of protection of the health and life of humans they intend to ensure and to impose safeguards of varying severity for that purpose. (30) The exclusive legislative power of the Member States extends, on the other hand — again subject to compliance with the fundamental principles of the Community legal order and having regard to the objectives pursued by the Directive — to MAs for parallel imports of medicinal products. And the latter field has likewise not been the subject of harmonisation.

20. That said, I think it is appropriate first of all to consider whether or not voluntary surrender of a currently valid MA by its holder can be regarded as being in conformity with the system established by the Directive. Essentially, that is not a point at issue in the main proceedings but the High Court referred to it in its second question (in subparagraph (i) — see point 13 above), asking whether that fact was relevant to the answer to be given to the first question. The doubt raised is legitimate in view of the wording of the abovementioned Article 21 of the Directive, according to which '[a]n authorisation to market a proprietary medicinal product shall not be refused, suspended or revoked except on the grounds set out in this Directive' (emphasis added; see points 4 and 5 above). The Commission, however, correctly observed that one of the fundamental principles of Community pharmaceutical legislation, to which the concept of compulsory licensing is entirely alien, is that the applicant is master throughout the procedure leading to the issue of an MA. The applicant is therefore entirely free to decide if and when to lodge an application, to withdraw an application before adoption of the final decision, and whether or not to apply for renewal of an authorisation that has expired (see Article 10 of the Directive). I do not therefore see how it can be contended that the holder is precluded from surrendering an MA which is still valid, that is to say relinquishing the benefit of a measure that is favourable to him and was granted primarily in his interests. I consider, therefore, that Article 21 is to be interpreted as relating only to cases of revocation in the strict sense, effected by the competent national authority against the wishes of the holder.

21. In that light, the interpretation requested by the High Court to enable it to give judgment is concerned essentially with the question whether, in circumstances like those of this case, the absence of significant differences in therapeutic efficacy between the old and new versions of the medicinal product is sufficient to relieve parallel importers of the obligation to provide the competent national authority with all the information prescribed by Article 4 of the Directive for monitoring the efficacy and harmlessness of the product in question, despite the fact that there is no valid 'mother' MA for the old version in the importing Member State. The United Kingdom authorities consider that to be the case: and they take that view — as they made clear at the hearing — regardless of the fact that the old version of Zimovane was previously covered by an MA of United Kingdom origin which is now inoperative. All that is important, they submit, is that the data, documents and details provided by RPR under the Directive in connection with the procedure for issue of the MA for the new version of Zimovane do not differ from those relating to the old version, which is intended to be the subject of parallel imports. (31) Besides, under paragraph 4(d) of the MAL 2 (PI), it is sufficient that the product to be imported by way of parallel import does not display differences which have an impact on the therapeutic effect as compared with a product covered by an original MA for the United Kingdom (see footnote 17 above). The United Kingdom submits that the position described here conforms with the rules for classifying different variants of a product as different medicinal products for the purposes of the marketing authorisation, which this Court laid down for the first time in De Peijper (see footnote 12 above and the relevant part of the text) and later referred to in paragraph 22 of Smith & Nephew. According to the United Kingdom, in addition the threefold rule laid down by the Court in Smith & Nephew should be interpreted as placing the emphasis on the active ingredient of the medicinal preparation. If on the other hand the rule in question were to be applied literally to every minor change in the formulation of a medicinal product, even those having no impact on its therapeutic effects, it could lawfully achieve the result of stopping parallel imports of the earlier version of the product. Moreover, according to the United Kingdom authorities, in Smith & Nephew the Court did not intend to lay down a rule that was universally applicable to all parallel imports but merely applied to the facts of that case the principles established in De Peijper. Therefore, the rule referred to is applicable only where the medicinal product brought in by way of parallel import and the product covered by an MA in the importing Member State are not manufactured by companies in the same group.

22. The objections raised are of some merit and substance. They bring to light the fundamental difference between a 'De Peijper type' situation (product of the same name produced by a single group of companies in several Member States, with national variants containing different excipients) and a 'Smith & Nephew' situation (product of the same name produced in several Member States under licence from a single producer, by manufacturers that are independent from each other, with national variants containing different excipients) and the effects which are associated with

that diversity from the legal point of view. In the first case it is legitimate to ask — as Advocate General Mayras did in the past — 'what interest a manufacturer of pharmaceutical products can have in manufacturing in different forms a medicinal preparation intended to be marketed under the same name in different countries and which, looked at purely from the point of view of rationalising production and costs, should be composed, prepared and checked in exactly the same way. There is no doubt that some of these different forms may be obligatory under specific national health rules. But even allowing for these rules, the question often remains unanswered, unless the view is taken that the differences in question were introduced for purely commercial reasons with a view to dividing up the market and taking advantage of a profitable situation'. I believe that in De Peijper Advocate General Mayras was suggesting to the Court, for the reasons set out here, that it should presume that any differences of formulation between the products in question, having, objectively, no therapeutic importance, can be accounted for only by an intention on the part of the manufacturer to isolate individual markets. (32) As the Court went on to say, those differences cannot therefore be regarded as relevant in determining whether or not the variant intended to be the subject of parallel imports has already been marketed in the importing Member State. Whilst pointing out that the solution of having the requirements of the free movement of goods take precedence over those of public health is a little dangerous, Advocate General Mayras took that view that in circumstances like those of De Peijper — having regard to the strong temptation facing manufacturers to exploit differing legislation in order to make huge profits and isolate markets — that solution involves a minor risk worth running. (33) That solution is clearly based on the proposition — which I think reflects the technical and scientific thinking of the time — that the fact that two medicinal products have the same therapeutic effect in itself implies that they are also the same as far as monitoring users' safety is concerned.

23. In its judgment in Smith & Nephew, however, the Court took the view, if I am not mistaken, that it is wholly legitimate for individual national licensees not linked by membership of the same group of companies to decide to manufacture medicinal products under licence according to different specifications, in particular as regards the excipients employed, without it being possible to attribute that fact, even merely by way of presumption, to a concerted intent to isolate the national markets. It should be remembered that S&N had been required to carry out additional clinical studies and to change the formulation (more precisely, the excipients used) of the Ditropan manufactured in the United Kingdom as compared with that produced in the United States by the licensor company, Marion Merrel Dow (and in Belgium by one of its subsidiaries), in view of the need to prove to the MCA that the product was not potentially carcinogenic. (34)

24. The Smith & Nephew judgment also recognised, at least by implication, that even where the differences of formulation as between the variants of a product are not reflected by differences in their respective therapeutic effects, those differences still fall within the range of factors of which the competent authority (subject to review by the national courts) must take into account when monitoring, the quality, safety and efficacy of the variants in question for the purpose of classifying them as similar or different medicinal products with a view to authorising their marketing. (35) As stated by the plaintiffs in the main proceedings, France and the Commission, the principle that the competent authority is required to take account not only of the therapeutic efficacy but also of the composition in terms of active ingredients and excipients of the various versions of a given medicinal product can be inferred from numerous pieces of legislation. I have already stated that the competent national authorities are required to examine applications for authorisation on the basis of the protocols described in the abovementioned annex to Directive 75/318 (footnote 6 above and the relevant part of the text). Pursuant to those protocols, the qualitative particulars of all the constituents of the proprietary medicinal product — which an applicant for an MA must supply in accordance with point 3 of the second paragraph of Article 4 of the Directive — consist in the designation or description not only of the active ingredients and of the constituents of the pharmaceutical form to be administered to the patient but also of the constituents of the excipients, whatever their nature or the quantity used (including colouring matter, preservatives, stabilizers, thickeners, emulsifiers, flavouring and aromatic substances). The constituents of the excipient of which details are needed for proper administration of the medicinal product also form part — again in the context of qualitative and quantitative composition — of the summary of product characteristics which must be supplied by an applicant for an MA (see point 9 of the second paragraph of Article 4 of the Directive). (36) The person concerned is also required to explain the function envisaged for the excipients in the finished product, at the same time providing scientific data relating to medical development. Also, in the context of the description of the method of preparation — which must accompany the application under point 4 of the second paragraph of Article 4 — the actual manufacturing formulation must give a quantitative breakdown of all the substances used, including the excipients (although for the latter approximate terms may be used 'in so far as the pharmaceutical form makes this necessary'). Moreover, the identification and dosage of the excipient constituents are part of the information relating to controls carried out on the finished product which the applicant is required to provide under point 7 of the second paragraph of Article 4 of the Directive. (37)

The introductory part of the annex to Directive 75/318 also provides that, in assembling the dossier, applicants must take into account the Community guidelines relating to the quality, safety and efficacy of medicinal products published by the Commission in its guide to the rules on medicinal products in the European Union.

From both the Commission‘s observations and from the latest edition of that guide, (38) it is apparent that changes to the formulation of a medicinal product affectingexcipients can affect the shelf-life and bioavailability of the product; (39) moreover,
the excipients can raise safety problems, and thus even where there is definite bio-equivalence between two medicinal products, they cannot necessarily be considered as equivalent as regards therapeutic effect (see footnote 38 above and the relevant part of the text). On the basis of the principles to which I have referred, the Court recognised in its recent judgment in the Generics case that one of the instances in which a generic product — although satisfying the requirement of having the same qualitative and quantitative composition in terms of active principles, the same pharmaceutical form and displaying bio-equivalence — cannot be regarded as 'essentially similar‘ to an original medicinal product for the purposes of admitting the second applicant for an MA to the abridged procedure provided for by Article 4.8(a)(iii) of the Directive is precisely a case in which it is apparent in the light of scientific knowledge that the product in question differs significantly from the original product as regards safety or efficacy in relation to the excipients which it contains. (40)
25. I wonder, at this stage, what considerations might possibly preclude the application to this case of the Smith & Nephew doctrine which, as I have just noted (point 24), has the merit of reflecting the results achieved following the most recent technical and scientific developments. The national court indicated in its first question (in subparagraph (iv)) that the holders of the MAs and the producers of the old and new versions of Zimovane are members of the same group of companies. It is therefore appropriate in this case to apply the presumption referred to in De Peijper (see point 22 above). I consider, however, that that rule needs to be clarified in an important respect. The United Kingdom proposes that it be applied automatically. More precisely, it interprets it as an irrebuttable presumption (juris et de jure), whereby two variants of a medicinal product having the same therapeutic effect must be treated as one and the same product. And that should always be the case: regardless of any differences in the excipients used or in the 'recipe‘ and whatever the reasons for such differences. I cannot agree with the United Kingdom's view.
26. As Advocate General Mayras noted in De Peijper, in this area it is necessary to seek a delicate balance between the opposing requirements of free movement of goods and protection of public health, between the aim of eliminating any State measure which reserves imports of a medicinal product to operators belonging to the official distribution network of the holder of the MA and the aim of ensuring strict monitoring of the efficacy and harmlessness of the products available on the national market, even though in some cases there may be duplication of the relevant administrative checks. Freedom of parallel imports must be duly safeguarded — and affects the applicability of the derogation under Article 36 of the EC Treaty (now, after amendment, Article 30 EC) to the restrictive measure, consisting of the need for an MA for the import of medicinal products which are already covered by an MA in another Member State — where it is apparent or can be inferred that the manufacturer of the different variants of a medicinal product intends partitioning the Community market and, in particular, isolating the national markets in which it might be able to charge the highest prices. That freedom should not however be seen as a dogma. In my view, therefore, the competent state authority will be required to treat as different products, for the purposes of MAs for the national market, the variants of a medicinal product with different formulations where recourse to that policy of diversification by the sole manufacturer appears to be based on genuine and objectively verifiable reasons relating to the protection of public health. It should also be noticed mutatis mutandis that even according to Smith & Nephew the obligation of the competent national authority of a Member State to extend the original MA granted in that State so as to cover a variant of a medicinal product that is (i) imported as a parallel import from another Member State in which its marketing is duly authorised and (ii) is identical to the one authorised in the importing Member State according to the three parameters laid down by the Court, does not apply where there are countervailing considerations relating to effective protection of the health and life of humans. (41)
27. I conclude therefore that the presumption established in De Peijper (differences of formulation without any impact on therapeutic effect = same level of quality and safety for users of the various national variants = intention of the manufacturer to divide up the market) is to be seen as a rebuttable presumption (juris tantum), which can be set aside in the face of evidence to the contrary. If the manufacturer is able to demonstrate to the full satisfaction of the competent national authority that the difference of formulation is a response to genuine and objective concerns of public health — and only in such circumstances — it will have to be concluded that the variants of the medicinal product in question are different products and that, in consequence, that authority does not possess for both certain information prescribed by the directive. I would add that the factors which the competent authority (and possibly the courts) of the importing Member State must take into account when assessing the gravity and reality of the grounds of protection of public health relied on by the manufacturer to justify the differences of formulation of the diverse variants include the possibility that the version withdrawn from the national market in question may nevertheless still being manufactured and marketed by the same firm or by a company in the same group in other Member States. Convincing reasons must therefore be given for that situation, including an explanation why those public health concerns do not arise in relation to the countries in question, or other factors such as, for example, the characteristics of the market for the medicinal product in question or the existence of particular contractual relationships in the

Member States concerned, otherwise the balance might be tipped towards the conclusion that the variants are substantially the same. As far as this case is concerned, it is not possible to identify, from the documents before the Court, the reasons for which an MA for the new version of Zimovane was not applied for in France, Greece, Italy and Spain (see point 11 and footnote 24 above). However, as the national court has observed, in this case it was the United Kingdom authorities themselves which stated that the purpose of developing and introducing the new formulation of Zimovane was not to isolate the United Kingdom market from the remainder of the Community (see point 16 above).

28. If it should be proved that the variations in the formulation of the different variants are intended to protect public health, there must be declared lawful under Article 36 of the EC Treaty (now, after amendment, Article 30 EC) any refusal by the competent national authority to allow under the simplified ad hoc procedure the parallel import of a medicinal product of the same name as that for which there is a valid MA in the importing Member State, even if the former has the same therapeutic effect and contains the same active principle as the latter. In any such case, in fact, it must be concluded, first, that the overriding requirement of the protection of public health and life of humans cannot be satisfied as effectively by means of measures which restrict Community trade to a lesser extent than the imposition on the parallel importer of the burden of applying for an MA in accordance with the provisions of the Directive. Second, in the circumstances described, there are no grounds for saying that the requirement of an MA for products imported from other Member States in which their release onto the market is authorised is being used so as to deviate from its true purpose with a view to discriminating in an arbitrary manner against medicinal products originating in other Member States or indirectly protecting domestic production. The solution which I suggest here, moreover, makes it possible to avoid a situation where the producers of a given medicinal product are able, by deliberately introducing some marginal change to the formulation of the product, to block parallel imports of a variant of that product which has been proved safe, as is feared by the United Kingdom authorities.

29. That said, it must be repeated that it is incumbent on the United Kingdom, after considering the degree of harmonisation of Community law in the area concerned, to establish, within the limits imposed by the Treaty, the level at which it intends to ensure protection of the life and health of humans within its territory (see footnote 28 above and relevant part of text). The MCA has decided that there are no doubts as to the harmlessness of the medicinal product at issue under normal conditions of use and that the reasons set out in the confidential annex, which in 1996 prompted RPR to market the new version of Zimovane and at the same time to withdraw the earlier version from circulation, cannot be linked with the general interest in ensuring the protection of human health, as that concept is understood in United Kingdom law. However, the applicability of Article 36 of the EC Treaty (now, after amendment, Article 30 EC) to this case was ruled out by the MCA because of the alleged absence of concrete proof of the factual circumstances giving rise to the concerns regarding the protection of public health mentioned by RPR rather than because it considered in the abstract that the reasons relied on by the plaintiffs were inadequate. Without prejudice to the fact that the final word remains with the national court when evaluating the views of the defendant administration, I would observe, in passing, that that administration does not appear in principle to dispute that checks on the safety of medicinal products placed on the market must extend to adverse side effects under actual conditions of use. That is, not by chance, a fundamental principle forming part of the Community rules on this matter. It is relevant to note the obligations mentioned by France and the Commission in their observations, which derive from the rules on the exchange of information and cooperation between national authorities in the area of pharmacovigilance. (42) In particular, Article 29a of Directive 75/319, under which the Member States are required to establish national systems for the collection and scientific evaluation of useful information concerning adverse reactions on the part of humans, provides that such systems must 'also collate information on frequently observed misuse and serious abuse of medicinal products‘. I agree, finally, with the submissions of the French authorities to the effect that the competent authority or the national courts of the importing Member State, in analysing the level at which the protection of human life and health is ensured in national law, are required to establish whether the precautionary principle and the principle that preventive action should be taken — principles analogous to those which, under the Treaty, apply to the action of the Community authorities — are applicable. (43)

**IV — Conclusions**

30. In view of all the foregoing considerations, I propose that the Court give the following answers to the questions referred to it by the High Court of Justice:

'Articles 30 and 36 of the EC Treaty (now, after amendment, Articles 28 and 30 EC, respectively) must be interpreted as meaning that any person proposing to import from Member State A into Member State B a medicinal product X, which uses the same active ingredient and has the same therapeutic effects but is manufactured according to a different formulation from that of a medicinal product Y, which is covered by a marketing authorisation in Member State B, is required to apply for and obtain a marketing authorisation from the competent authorities of Member State B in accordance with and for the purposes of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, as amended, where:

(i) medicinal product X is the subject of an MA granted in Member State A but not an MA granted in Member State B,

(ii) medicinal product Y is the subject of an MA granted in Member State B but not of an MA granted in Member State A,

(iii) the marketing authorisations mentioned under (i) and (ii) above were granted to different members of the same group of companies and the manufacturers of the medicinal products X and Y are also members of that group of companies,

(iv) the formulation of medicinal product Y was developed and introduced in order to secure a public health benefit which medicinal product X (produced according to a different formulation) does not provide,

(v) it is not possible to secure that public health benefit where medicinal product X and medicinal product Y are available at the same time on the market of Member State B, and

(vi) companies in the same group as the holder of the MA for medicinal product X continue to manufacture and market that product in Member States other than Member State B, provided that the holder of the MA is able to prove, on the basis of objective justifications, that the marketing of medicinal product X in those Member States does not present public health risks similar to those to which it would give rise in Member State B.‘

In the absence of Community harmonisation of national requirements for the placing of parallel imports of medicinal products on the market, it is incumbent on the authority responsible for issuing marketing authorisations,

and if appropriate the national courts, to determine whether the reasons for which the formulation of medicinal product Y was developed and introduced can be linked with the general interest in protecting human life and health, as that concept is understood in national law.

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1: Original language: Italian.

2: — OJ English Special Edition 1965-66, p. 20. The amendments to the directive which are relevant here are those made by the following instruments: Second Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 L 147, p. 13; see Articles 35 and 36); Council Directive 83/570/EEC of 26 October 1983 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of the provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1983 L 332, p. 1; see Article 1(1) to (6)); Council Directive87/21/EEC of 22 December 1986 amending Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1987 L 15, p. 36; see Article 1(1)); Council Directive 89/341/EEC of 3 May 1989 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC (OJ 1989 L 142, p. 11; see Article 1(1) to (4)); and Council Directive 93/39/EEC of 14 June 1993 amending Directive 65/65/EEC, 75/318/EEC and 75/319/EEC (OJ 1993 L 214, p. 22; see Article 1). Directive 93/39 established, with effect from 1 January 1995, a decentralised procedure for mutual recognition of national marketing authorisations, together with binding arbitration by the Community in the event of disagreement between Member States (see Article 4, second paragraph, subparagraph 11, Article 7(2) and 7(a) of Directive 65/65/EEC and Articles 8 to 15c of Directive 75/319/EEC). The independent national procedures remain, but as from 1 January 1998 (the end of the transitional period for the new procedure) they are strictly limited to the initial phase (issue of the marketing authorisation by the 'reference Member State‘ and to medicinal preparations not marketed in more than one Member State.

3: — The abovementioned Directives 89/341/EEC and 93/39/EEC (see footnote 1 above), however, were adopted on the basis of Article 100a of the EC Treaty (now, after amendment, Article 95 EC).

4: — See the preamble to Directive 65/65/EEC (cited above, footnote 1, and relevant part of text), in particular the first recital.

5: — Or a Community MA granted in accordance with Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products (OJ 1993 L 214, p. 1).

6: — As the Court has emphasised (see Case C-440/93 Scotia Pharmaceuticals [1995] ECR I-2851, paragraphs 21 to 25), the discretion available to the competent authority for issue of authorisations in a Member State is rather limited in the context of the Directive. There is thus no possibility of issuing an MA when all the information specified in Article 4 has not been provided or the prescribed tests have not been carried out (fisico-chemico, biological or microbiological, pharmacological and toxicological, and clinical tests).

7: — See Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products (OJ 1997 L 147, p. 1). In order to facilitate the issue of marketing authorisations for the same medicinal product in several Member States, Directives 75/318/EEC and 75/319/EEC (cited in footnote 1 above) harmonised the methods for controlling medicinal products put on to the market, in particular by requiring the national authorities to examine applications for authorisation on the basis of the protocols described in the annex referred to in the text. That annex was replaced by Commission Directive 91/507/EEC of 19 July 1991 amending the annex to Directive 75/318/EEC (OJ 1991 L 270, p. 32) in order to bring it into line with technical progress.

8: — See Case 104/75 De Peijper [1976] ECR 613, paragraph 25.

9: — According to the said Article 30 EC, 'the provisions of Articles 28 and 29 shall not preclude prohibitions or restrictions on imports ... justified on grounds of ... the protection of health and the life of humans ... Such prohibitions or restrictions shall not, however, constitute a means of arbitrary discrimination or a disguised restriction on trade between Member States'. The Court has consistently held that Article 36 of the EC Treaty (now, after amendment, Article 30 EC) remains applicable to the production and marketing of pharmaceutical products until the national provisions have been entirely harmonised (see, amongst many, Case 215/87 Schumacher [1989] ECR 617, paragraph 15, Case C-369/88 Delattre [1991] ECR I-1487, paragraph 48, Case C-347/89 Eurim-Pharm [1991] ECR I-1747, paragraph 26, Case C-62/90 Commission v Germany [1992] ECR I-2575, paragraph 10, Case C-317/92 Commission v Germany [1994] ECR I-2039, paragraph 14, and Case C-320/93 Ortscheit [1994] ECR I-5243, paragraph 14.

10: — It should be noted that the medicinal product imported by the appointed distributor for the Netherlands and the one marketed by the parallel importer had common origins: they were produced — in Switzerland and the United Kingdom — by manufacturers belonging to the same group of companies.

11: — In De Peijper, the Netherlands judge asked the Court (I) whether Article 30 of the EC Treaty (now, after amendment, Article 28 EC) was to be interpreted as meaning that a national measure which makes the grant of the MA for a medicinal product subject to the condition that the parallel importer must provide the competent authority with documents identical to those already lodged by the manufacturer or his exclusive concessionaire is compatible with that article, where: (i) the medicinal product in question, prepared in accordance with uniform methods and having a homogeneous qualitative and quantitative composition, is marketed in one or more Member States on the basis of proper authorisations, (ii) in each of those Member States the competent authority informed third parties of the grant of the MA by means of appropriate official publication, (iii) an operator established in one of those Member States who intends making parallel imports of the medicinal product in question can obtain the data concerning the preparation and qualitative and quantitative composition of it only if the producer or official distributors in the importing State are prepared to provide him with them, and (iv) the health authorities of that State already hold the relevant documents, produced at an earlier stage in support of the application for the MA; and (II) whether the answer given to the first question was also valid where there were differences between the product authorised in the Member State of importation and the product of the same name imported in parallel from another Member State (differences concerning the manufacturing processes or the qualitative and quantitative composition), which were irrelevant such that 'it is likely that the manufacturer ... [had the] ... exclusive intention of using the differences ... in order to prevent or impede the possibility of the parallel importation' (see De Peijper, cited in footnote 8, paragraphs 10, 11 and 33).

12: — See De Peijper (cited in footnote 8 above), paragraph 18.

13: — See paragraphs 20 to 32. The Court, first, made it clear that the derogation under that article cannot be invoked regarding the parallel importer's obligation to produce a document such as the file provided for by the Netherlands legislation: 'If the public health authorities of the importing Member State already have in their possession, as a result of importation on a previous occasion, all the pharmaceutical particulars relating to the medicinal preparation in question and considered to be absolutely necessary for the purpose of checking that the medicinal preparation is effective and not harmful, it is clearly unnecessary, in order to protect the health and life of humans, for the said authorities to require a second trader who has imported a medicinal preparation which is in every respect the same to produce the abovementioned particulars to them again' (paragraph 21, emphasis added). As regards, on the other hand, the obligation to produce documents like the records for each batch of products imported in parallel, the Court observed that it is undeniable that the national competent authorities must be able to verify, with absolute certainty and at any time, whether or not a particular batch conforms with the information given in the file. However, according to the Court, even where the administrative rules in force in the importing Member State include the requirement that a parallel importer must prove that an imported batch conforms to the description of the medicinal product, there would '... be no justification under Article 36 [now, after amendment, Article 30 EC] for compelling him [to produce] documents to which he does not have access when the administration, or as the case may be, the court, finds that evidence can be produced by other means', such as the exchange between national administrations of 'the documents necessary for checking certain largely standardised and widely distributed products' (see paragraphs 29 and 27).

14: — See paragraph 36 of the grounds and paragraph 3 of the operative part.

15: — See proposal for an amendment of Directive 65/65/EEC and 75/319/EEC of 2 June 1980 (OJ 1980 C 143, p. 8).

16: — See Commission communication on parallel imports of proprietary medicinal products for which marketing authorisations have already been granted (OJ 1982 C 115, p. 5).

17: — See Notes on Application for Product Licences (Parallel Importing) (Medicines for Human Use), as amended (hereinafter 'MAL 2 (PI)').

18: — Under Paragraph 4 of MAL 2 (PI), the medicinal product sought to be imported by way of parallel import must be:

(a) a product which is to be imported from a Member State of the European Communities;

(b) a proprietary medicinal product (as defined in Article 1 of the Directive) for human use;

(c) covered by a valid MA granted in accordance with Article 3 of the Directive by the regulatory authority of a Member State;

(d) have no differences, having therapeutic effect, from a product covered by a United Kingdom MA;

(e) made by or under licence to: (i) the manufacturer who made the product covered by the UK MA or (ii) a member of the same group of companies.

If even one of those conditions is not met, the application for the PL(PI) cannot be granted and the applicant is invited to apply for an MA under the normal procedure (MAL 2). Pursuant to paragraph 12 of MAL 2 (PI), a PL(PI) remains in force only so long as both the United Kingdom MA (sometimes referred to as the reference or 'mother' authorisation) and the Community reference MA are in force. If either ceases to be valid for any reason (for example, it may lapse or be revoked) the PL(PI) also ceases to be valid. Paragraph 21 of MAL 2 (PI) provides, finally, that the normal arrangements apply with regard to variations to a PL(PI) made at the request of the licence holder. The competent authority verifies that the terms of the authorisation still conform with the relevant provisions of the applicable MA and notifies the PL(PI) holder of any action necessary as a result of a variation to the United Kingdom reference MA. The holder of a PL(PI) is required to notify the competent authority of any variation to the Community MA that comes to his attention and is required to obtain a variation to the PL(PI) before he can market the varied product in the United Kingdom.

19: — See Case C-201/94 Smith & Nephew and Primecrown [1996] ECR I-5819.

20: — More specifically, the United States company Marion Merrel Dow had licensed the right to produce and market the medicinal product Ditropan to S&N for the United Kingdom and to Marion Merrel Dow Belgium for Belgium.

21: — See Case C-201/94 (cited above, footnote 18), paragraphs 19 to 21.

22: — See Case C-201/94 (cited above, footnote 18), paragraph 25.

23: — See paragraph 1 of the operative part of the judgment in the same case. 'It would therefore be contrary to [the Directive]' the Court observed, '... for a competent national authority, in the context of an application for a marketing authorisation falling within the scope of that Directive, to use information supplied by an independent company, without its agreement, in support of an application for a marketing authorisation concerning another proprietary medicinal product' (see, ibid., paragraph 31).

24: — They are authorisations numbers 0012/0162 (Zimovane 7.5 mg tablets), 0012/0163 (Zimovane in 3.75 mg capsules), 0012/0164 (Zimovane in 7.5 mg capsules), 0012/0259 (Zolerim in 7.5 mg tablets) and 0012/0260 (Zimovane in 3.75 mg tablets). Only marketing authorisation number 0012/0162 was in fact used.

25: — RPR'S representative stated at the hearing that an MA for the new version of Zimovane has already been granted in Sweden, and the old version would no longer be distributed in that country. An MA for the new version of Zimovane has been applied for in eight further Member States (Ireland, Denmark, France, Germany, Belgium, Luxembourg, Finland and the Netherlands) and in Norway.

26: — Under Article 29d of Directive 75/319/EEC, the person responsible for placing the medicinal product on the market is required (i) to report all suspected serious adverse reactions which are brought to his attention by a health care professional to the competent authorities without delay and (ii) to maintain detailed records of all other suspected adverse reactions, accompanied by a scientific evaluation, presenting the same to the competent authorities immediately on request or at least every six months for the first two years following authorisation, and once a year for the following three years. Before giving a decision on a request for renewal of an MA the competent authority must in addition examine a file containing up-to-date pharmacovigilance data (see Article 10, first paragraph, of Directive 65/65). I think it is also appropriate to note here the provisions of Article 4b, second paragraph, and Article 7, second paragraph, of Directive 65/65, which, for the dual purpose of ensuring better protection of pubic health and avoiding pointless duplication in the examination of applications for MAs require the Member Statessystematically to draw up evaluation reports for every medicinal product authorised by them, to exchange them on request when in respect of a medicinal product already authorised in one Member State there is an application pending for an MA in another Member State and to update them whenever new information is received that is relevant to evaluation of the quality, safety or efficacy of the medicinal product in question.

27: — It has been rightly pointed out that a medicinal product is a paradoxical product in the sense that although its essential function is clearly therapeutic it may also give rise to pathological conditions if it is defective or misused (see E. Cadeau and J.-Y. Richeux, 'Le Juge Communautaire et le Médicament. Libre Circulation des Marchandises et Protection de la Santé Publique' in Les Petites Affiches No 7/1996, p. 4).

28: — But see footnotes 1 and 5 above.

29: — See Case C-320/93 Ortscheit, cited above, footnote 8, paragraph 18.

30: — Ibid., paragraph 16, and paragraph 15 of the 1976 case cited in footnote 7 above.

31: — The United Kingdom authorities seem, therefore, implicitly to admit in principle that in the event of revocation (or non-renewal) of an original MA or voluntary surrender not followed by an application for an MA for a different variant of the medicinal product in question, it is not in any event permissible to authorise on the basis of MAL 2 (PI) parallel imports of the product from other Member States in which it is covered by valid authorisations, with the result that it is necessary for the MCA to undertake the procedure for complete evaluation provided for by the Directive.

32: — See the Opinion of Advocate General Mayras in De Peijper [1976] ECR 641, particularly at 650 and 651.
33: — Ibid.
34: — Smith & Nephew, cited in footnote 18 above, paragraph 9.
35: — It should be borne in mind that the 'criteria of quality, safety and efficacy' are those on which, in the interests of public health and for the benefit of users of the medicinal products, the decision of the competent national authority on an application for an MA must be exclusively based (see the third recital in the preamble to Directive 93/39, cited in footnote 1 above).
36: — The summary of the product characteristics must contain the information listed in Article 4a of the Directive. Under Article 4b, when the marketing authorisation is issued the person responsible for placing that product on the market is to be informed, by the competent authorities of the Member State concerned, of the summary of the product characteristics as approved by them. The competent authorities are to take all necessary measures to ensure that the information given in the summary is in conformity with that accepted when the marketing authorisation is issued or subsequently.
37: — See the Annex to Directive 75/318 (cited in footnote 6), paragraph 3, part 2, points A.1.1., A.4.1, B.1 and E.1.3.
38: — See European Commission, The Rules governing medicinal products in the European Union, Volume IIIC, Guidelines on the quality, safety and efficacy of medicinal products for human use. Efficacy, Luxembourg 1998, pp. 233-235.
39: — Bio-availability means the proportion of active substance or therapeutic moiety (for example salts, esters, etc.) delivered from a pharmaceutical form which reaches the central circulatory system of a patient to whom the medicinal product is administered. Differences in the excipients and/or in the production process for two medicinal products may lead to differing rates of dissolution or absorption. Two medicinal products, which are 'pharmaceutical equivalents' (that is to say they contain the same quantity of the same active substance in the same dosage forms) or 'pharmaceutical alternatives' (having the same therapeutic moiety but in a different chemical form or dosage form) are said to be bio-equivalent if their respective bio-availabilities are so similar as to give rise to essentially identical effects in terms of efficacy and safety. In practice, the proof of bio-equivalence between pharmaceutical equivalents or alternatives is also the most adequate proof of therapeutic equivalence as between the medicinal products in question, provided that they contain excipients generally recognised as safe and bear the same instructions for use (ibid.).
40: — See Case C-368/96 The Queen v The Licensing Authority established by the Medicines Act 1968, ex parte Generics [1998] ECR 0000, paragraphs 32, 33 and 36. The abovementioned point 8(a) of the second paragraph of Article 4 provides for three alternatives in which the applicant for an MA is not required to furnish the results of pharmacological and toxicological tests or of clinical trials. The abridged procedure referred to in the text, however, 'in no way relaxes the requirements of safety and efficacy which must be met by medicinal products' (see Case C-440/93, cited in footnote 5 above, paragraph 17). A generic medicinal product is a copy of an innovative medicinal product whose formulation can be reproduced by other manufacturers and which can be sold under the same name at a price that is usually lower than that of the original product.
41: — See Smith & Nephew, cited above (footnote 18), paragraph 1(a) of the operative part.
42: — See Article 29a to 29i of Directive 75/319, introduced by Article 3(3) of Directive 93/39 (cited in footnote 1 above).
43: — It follows from the principles mentioned in the text that, where there are uncertainties regarding the existence or scope of risks to consumers' health, the institutions may adopt protective measures without having to wait until the reality and seriousness of those risks have become fully apparent (see Case C-157/96 R v MAFF, ex parte National Farmers' Union and Others [1998] ECR I-2211, paragraph 63, and Case C-180/96 United Kingdom v Commission [1998] ECR I-2265, paragraphs 99 and 100).