OPINION OF ADVOCATE GENERAL LÉGER

delivered on 24 November 2005 [1]

1. Is there a 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products [2] in the case of a medicinal combination of two substances, one of which is a known substance with pharmacological properties of its own and the other makes it possible to increase significantly the therapeutic effects of the first substance?

2. This is essentially the question raised by the Bundesgerichtshof (Federal Court of Justice) (Germany) in an appeal brought by the Massachusetts Institute of Technology against the refusal by the German Patent and Trade Mark Office to grant it a supplementary protection certificate for the medicinal product Gliadel 7.7 mg Implant ('Gliadel'), composed of an active ingredient, carmustine, and a polymeric, biologically degradable excipient, polifeprosan ('the combination at issue'). [3]

3. After the Court has been required to give rulings in a number of disputes on the validity and the interpretation of Regulation No 1768/92, [4] in the present case it is being asked to consider the concept of 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Regulation No 1768/92.

I — Legal framework

4. Regulation No 1768/92 introduces a supplementary protection certificate, which is ancillary to a previously granted national or European patent, with a view to extending the duration of the rights that the patent confers on its holder. [5]

1 — Original language: French.

2 — OJ 1992 L 182, p. 1.

3 — The terms 'active ingredient' and 'excipient' are defined in points 10 and 11 of this Opinion.

4 — See Case C-350/92 *Spain* v *Council* [1995] ECR I 1985, Case C-181/95 *Biogen* [1997] ECR I-357, Case C-110/95 *Yamanouchi Pharmaceutical* [1997] ECR I-3251, and Case C-392/97 *Farmitalia* [1999] ECR I-5553.

5 — As the Court stated in paragraph 27 of the judgment in Case C-350/92 *Spain* v *Council*, cited above, this supplementary protection certificate does not create a new industrial property right.

5. The aim of the regulation is to play a role in the continuing improvement in public health by encouraging pharmaceutical research and innovation through the grant of supplementary legal protection to medicinal products that are the result of long, costly research (first and second recitals).

6. Pharmaceutical research activities require substantial investment which can be covered only if the undertaking carrying out the research gains a monopoly for the exploitation of its results for a sufficient period of time. In order to protect public health, placing a proprietary medicinal product [6] on the market requires authorisation to be granted, [7] at the end of a lengthy and complex procedure, with the result that the period that elapses between the filing of the application for a patent and the grant of authorisation to place the product on the market reduces significantly the duration of the exclusive exploitation rights, discourages investors and penalises pharmaceutical research [8] (third and fourth recitals). Such a situation gives grounds for fears that research centres situated in the Member States might relocate to countries that offer greater protection [9] (fifth recital).

7. In order to reduce the risk of the heterogeneous development of national laws which would be likely to create obstacles to the free movement of medicinal products in the internal market, Regulation No 1768/92 therefore introduces a certificate granted, under the same conditions, by all the Member States at the request of the holder of a national or European patent (sixth and seventh recitals).

8. Furthermore, in order to grant adequate effective protection for medicinal products equivalent to that enjoyed by other techno-

6 — Under Article 1(1) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ 2001 L 311, p. 67), 'proprietary medicinal product' means any ready-prepared medicinal product placed on the market under a special name and in a special pack. For information, it should be noted that the directive has recently been amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 (OJ 2004 L 136, p. 34) and by Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83 (OJ 2004 L 136, p. 85).

7 — With regard to the authorisation procedure for placing medicinal products on the market, see 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 (OJ, English Special Edition 1965-1966, p. 20), amended and supplemented by Second Council Directive 75/319/EEC of 20 May 1975 (OJ 1975 L 147, p. 13). These two pieces of legislation were replaced by Directive 2001/83.

8 — The duration of the protection granted by a patent in Europe is generally 20 years as from the date of filing of the application (see, with respect to European patents, Article 63(1) of the Convention on the grant of European patents (European Patent Convention) of 5 October 1973, 'the Munich Convention'). However, on account of the many physico-chemical, biological/microbiological, toxicological, pharmacological and clinical tests that must be conducted by an applicant for authorisation to place a product on the market, the procedure for the grant of such authorisation can last around 12 years. The pharmaceutical industry therefore has a period of only around eight years to exploit the patent. This situation is the result of administrative procedures which are moreover recognised and regarded as necessary in order to protect the public in connection with the marketing of medicinal products.

9 — In particular the United States of America and Japan.

logical sectors, [10] the regulation sets at 15 years the duration of the exclusive rights enjoyed by the holder of both a patent and a certificate from the time the medicinal product in question first obtains authorisation to be placed on the market in the Community (eighth recital).

9. Article 1 of Regulation No 1768/92 reads as follows:

'For the purposes of this regulation:

(a) "medicinal product" means any substance or combination of substances presented for treating or preventing disease in human beings or animals and any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in humans or in animals;

(b) "product" means the active ingredient or *combination of active ingredients of a medicinal product* [11];

(c) "basic patent" means a patent which protects a product as defined in (b) as such, a process to obtain a product or an application of a product, and which is designated by its holder for the purpose of the procedure for grant of a certificate;

...'

10. The concept of 'active ingredient' is not defined in Regulation No 1768/92. It designates a substance, such as a chemical compound or a natural solution, with pharmacological or physiological properties on which the therapeutic effect is based. [12]

11. This concept must be distinguished from 'excipient'. According to the list of reference

10 — This concern is now reflected in Article 27(1) of Annex 1C to the Agreement Establishing the World Trade Organisation, entitled 'Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)', which entered into force on 1 January 1995. That article provides that patent rights must be 'enjoyable without discrimination as to ... the field of technology ...'. All the Member States and the Community itself, for matters within its competence, are bound by the TRIPS Agreement, which was approved by Council Decision 94/800/EC of 22 December 1994 concerning the conclusion on behalf of the European Community, as regards matters within its competence, of the agreements reached in the Uruguay Round multilateral negotiations (1986-1994) (OJ 1994 L 336, p. 1).

11 — My emphasis.

12 — See Article 3(3)(a) of Commission Regulation (EC) No 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts 'similar medicinal product' and 'clinical superiority' (OJ 2000 L 103, p. 5).

terms in the European Pharmacopoeia, drawn up under the aegis of the Council of Europe,[13] an excipient is an auxiliary substance, generally therapeutically inert, and needed for the manufacture, administration or conservation of the active ingredient. Its function is to act as a vector or carrier for the active ingredient, thereby contributing to certain properties of the product, such as its stability, its galenical form[14] or its acceptability for the patient.

12. Article 2 of Regulation No 1768/92 defines the scope of the regulation as follows:

'Any product protected by a patent in the territory of a Member State and subject, prior to being placed on the market as a medicinal product, to an administrative authorisation procedure ... may ... be the subject of a certificate.'

13. Article 3 of the regulation sets out the conditions for obtaining a certificate. The 'product' must be protected by a basic patent in force in the Member State in which the application is submitted, a valid authorisation to place the product on the market as a medicinal product must have been granted, the product must not have already been the subject of a certificate and the abovementioned authorisation must be the first authorisation to place the product on the market as a medicinal product.

14. Article 4 of the regulation, which defines the subject-matter of the protection granted by the certificate, reads as follows:

'Within the limits of the protection conferred by the basic patent, the protection conferred by a certificate shall extend only to the product covered by the authorisation to place the corresponding medicinal product on the market and for any use of the product as a medicinal product that has been authorised before the expiry of the certificate.'

15. Under Article 5 of the regulation, 'the certificate shall confer the same rights as conferred by the basic patent and shall be subject to the same limitations and the same obligations'.

16. Lastly, under Article 13 of Regulation No 1768/92, the certificate takes effect upon

13 — Council Decision 94/358/EC of 16 June 1994 accepting, on behalf of the European Community, the Convention on the elaboration of a European Pharmacopoeia (OJ 1994 L 158, p. 17). Previously known as the Codex, the pharmacopoeia is an official collection for pharmacists containing the nomenclature and descriptions of medicinal products.

14 — Galenical pharmacy is a science for finding, for each active ingredient, the medicinal form most suitable for the treatment of a specific illness. The galenical form of a medicinal product is its mode of presentation (tablet, syrup, ointment, capsule, suppository, powder, etc.) and the way in which it is absorbed by the organism (sustained release, gastro-resistant, etc.).

the expiry of the basic patent for a period equal to the period which elapsed between the date on which the application for a patent was lodged and the date of the first authorisation to place the product on the market in the Community reduced by a period of five years. However, the duration of the certificate may not exceed five years from the date on which it takes effect.

II — Facts and main proceedings

17. The appellant in the main proceedings, the Massachusetts Institute of Technology ('MIT'), is the holder of a European patent ('the basic patent') the application for which was filed on 29 July 1987. One of the claims in that patent, the eighth, concerns 'a composition comprising a matrix of high molecular weight ... and a biologically active substance'.

18. By a decision of 3 August 1999, a marketing authorisation was granted in Germany for Gliadel which, I would recall, is composed of an active substance, carmustine, and a polymeric, biodegradable excipient, polifeprosan.

19. According to the basic patent, polifeprosan was developed to provide a biodegradable matrix for use in biomedical applications, especially for the controlled release of active substances in vivo. [15] Carmustine is a highly cytotoxic active substance, used for many years with inert vehicles and drug excipients in intravenous chemotherapy, in particular for the treatment of brain tumours (malignant glioma). According to the appellant in the main proceedings, usage of this active ingredient has not thus far made it possible to extend the life expectancy of patients significantly.

20. Gliadel is used to treat recurrent brain tumours in addition to surgery. It takes the form of a macroscopic disk which is implanted in the cranium after the surgical resection of the brain tumour. Its mechanism of action consists in the slow release of the active substance, controlled by polifeprosan, in order to delay the recurrence of the tumour. According to the appellant in the main proceedings, the combined use of carmustine and polifeprosan extends the life expectancy of patients by several months, by permitting the delivery of a much higher, but still constant, dose of the active substance onto the tumour bed.

15 — See the order for reference, English version, p. 3, and the description of the basic patent, p. 2 and 3.

21. MIT applied to the German Patent and Trade Mark Office (Deutsches Patent und Markenamt) for a supplementary protection certificate for Gliadel. In its main application, it requests that a certificate be granted for carmustine in combination with polifeprosan. Its alternative application seeks the grant of a certificate for carmustine only.

22. The German Patent and Trade Mark Office rejected the main application in its decision of 16 October 2001 on the ground that polifeprosan cannot be considered to be an active ingredient within the meaning of Article 1(b) and Article 3 of Regulation No 1768/92. It also ruled that no certificate could be granted for carmustine on its own in so far as carmustine had been an authorised active substance for many years. [16]

23. The appellant in the main proceedings lodged a complaint against that decision, which was rejected by the Bundespatentgericht (Federal Patent Court) in its decision of 25 November 2002. In its view, the conditions for obtaining a certificate are not fulfilled in the present case, since the combination of carmustine and polifeprosan is not a 'product' within the meaning of Article 1(b) of Regulation No 1768/92. It considers that 'combination of active ingredients of a medicinal product' within the meaning of that article necessarily requires the presence of two active ingredients, each with its own therapeutic effects. Gliadel has only one active ingredient, carmustine.

24. MIT then lodged an appeal with the Bundesgerichtshof against the decision of the Bundespatentgericht rejecting the complaint. In support of its appeal, the appellant in the main proceedings claims that polifeprosan is neither an excipient nor a mere auxiliary component. It considers that polifeprosan is an essential component of Gliadel since it enables carmustine to be administered in a therapeutically relevant way for the treatment of malignant brain tumours, thereby contributing to the efficacy of the medicinal product. According to MIT, the controlled release of carmustine, which, moreover, would have a lethal effect were it released in a single dose due to its high toxicity, is not possible without the use of the biodegradable substance.

III — The questions referred for a preliminary ruling

25. The Bundesgerichtshof has doubts as to the interpretation to be given to the concept of 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Regulation No 1768/92.

16 — By way of information, the first authorisation to place carmustine on the market was granted on 6 March 1979 in the United Kingdom.

26. It points out, first of all, that the terms 'active ingredient' and 'combination of active ingredients' are Community law notions which must, as such, be interpreted autonomously. [17] It notes that these terms are not defined either in Regulation No 1768/92 or in the Court's case-law.

27. The referring court then explains that 'combination of active ingredients' can give rise to two interpretations.

28. The Bundesgerichtshof considers that the concept can be interpreted as meaning that each of the components of this combination is an active ingredient with its own therapeutic effects.

29. In this respect it points out the distinction drawn by Regulation No 1768/92 between the terms 'medicinal product' and 'product'. The referring court states that Article 1(a) of that regulation defines 'medicinal product' as '*any substance or combination of substances*[18] presented for treating or preventing disease in human beings or animals'. It notes that, on the other hand, Article 1(b) of the regulation defines 'product' as '*the active ingredient* or combination of *active ingredients*[19]' of a medicinal product. In the view of the Bundesgerichtshof, the distinction between these two expressions could be evidence that only active ingredients or combinations of two or more active ingredients making up a medicinal product come under the term 'product'. Since polifeprosan is only an excipient which does not itself have any therapeutic effect, it would not therefore be possible to grant the certificate requested by MIT.

30. The referring court has doubts as to this first interpretation, however. It notes that in the explanatory memorandum for its proposal for a regulation [20] the Commission of the European Communities states that all pharmaceutical research which may be patented, whether it concerns a new product, a new process for obtaining a new or known product, a new application of a product or a new combination of substances containing a new or known product, must be encouraged. In the view of the referring court, it could therefore be assumed that the combination of a new excipient with a known active substance will be eligible for the grant of a supplementary protection certificate if

17 — The referring court cites the judgment in Case C-449/93 *Rockfon* [1995] ECR I-4291, paragraph 28

18 — My emphasis

19 — My emphasis

20 — Proposal for a Council Regulation (EEC) concerning the creation of a supplementary protection certificate for medicinal products (COM(90) 101 final — SYN 255, 11 April 1990, point 29(2), 'the Commission's explanatory memorandum')

this combination results in a new medicinal product in which the therapeutic effects of the active ingredient are defined and controlled by the additional substance.

31. The Bundesgerichtshof notes that this latter interpretation has already been adopted in some Member States of the Community in so far as the French Republic and the United Kingdom have granted a supplementary protection certificate for the combination at issue. [21]

32. In the light of these considerations, the Bundesgerichtshof decided to stay the proceedings and to refer the following questions to the Court for a preliminary ruling:

'(1) Does the concept of "combination of active ingredients of a medicinal product" within the meaning of Article 1(b) of Regulation No 1768/92 mean that the components of the combination must all be active ingredients with a therapeutic effect?

(2) Is there a "combination of active ingredients of a medicinal product" also where a combination of substances comprises two components of which one component is a known substance with a therapeutic effect for a specific indication and the other component renders possible a pharmaceutical form of the medicinal product that brings about a changed efficacy of the medicinal product for this indication (in vivo implantation with controlled release of the active ingredient to avoid toxic effects)?'

IV — Analysis

33. With these two questions referred for a preliminary ruling, which should be examined together, the referring court is essentially asking the Court whether the concept of 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Regulation No 1768/92 must be interpreted as including a combination of two substances, only one of which has pharmacological properties of its own for a specific therapeutic indication and the other is necessary for the therapeutic efficacy of the first substance, for this indication.

34. The issue arises in so far as Article 1(b) of the regulation, which defines the term 'product', mentions only 'the active ingredient or combination of active ingredients of a medicinal product'.

21 — It can be seen from the order for reference, English version (p. 4), that the combination of carmustine and polifeprosan already has a supplementary protection certificate in France (since 7 July 2000) and in the United Kingdom (since 16 January 2003).

35. This restrictive definition has its origin in the fact that, as has been pointed out, the main purpose of Regulation No 1768/92 is to extend, up to a maximum of five years, the monopoly for the exploitation of a product conferred by a patent on its holder. This supplementary protection therefore delays by the same period the date from which the product in question comes into the public domain and may be competitively marketed.

36. The Bundesgerichtshof therefore asks whether the scope of the supplementary protection certificate should extend to a combination like the one at issue in the main proceedings.

37. I believe that this question should be answered in the affirmative.

38. Whilst Article 1(b) of Regulation No 1768/92, as it is worded, means in principle a combination of two or more active substances, I do not think that a purely literal interpretation of that provision allows a combination comprising an active ingredient and an excipient to be disqualified from classification as a 'product' within the meaning of the regulation in the specific case where the excipient is necessary for the therapeutic efficacy of the active ingredient. [22]

39. Such a restrictive interpretation of the provision at issue would not be consistent either with the broad logic of the regulation of which it forms part or, above all, with the objectives pursued by the Community legislature.

A — *The broad logic of Regulation No 1768/92*

40. As has been pointed out, Regulation No 1768/92 establishes a system of protection *supplementary* to that granted by a basic patent. As is evident from Articles 3, 4 and 5 of the regulation, the certificate is closely linked to the national or European patent previously granted and to the marketing authorisation granted by the competent national authorities.

22 — None of the other language versions of the regulation dispels my doubts as to the interpretation of that provision. The versions, including the French ('composition de principes actifs d'un médicament'), German ('Wirkstoffzusammensetzung eines Arzneimittels'), Spanish ('composición de principios activos de un medicamento'), Italian ('composizione di principi attivi di un medicinale'), and Dutch ('samenstelling van werkzame stoffen van een geneesmiddel') are similar to the English version.

41. First of all, under Article 3(a) and (b) of the regulation, the certificate may be granted only if the product in question is both protected by a basic patent and authorised to be placed on the market.

42. Secondly, in accordance with Article 4 of the regulation, the protection conferred by the certificate extends only within the limits of the protection conferred by the patent and only to the product covered by the marketing authorisation.

43. Lastly, and above all, under Article 5 of the regulation, the holder of the certificate not only enjoys the *same rights* as conferred by the basic patent, but is also subject to the *same limitations* and the *same obligations* laid down by the patent. [23]

44. Indeed, the supplementary protection certificate is the natural extension of the basic patent. In these circumstances, in my view there is nothing to prevent a medicinal combination which is not only protected by a patent but has also been granted a marketing authorisation from enjoying supplementary protection if that combination is also among the therapeutic innovations whose development Regulation No 1768/92 seeks to encourage. [24]

45. It follows that, far from precluding the grant of a supplementary protection certificate to a combination like the one at issue in the main proceedings, which is covered by a basic patent and is authorised to be placed on the market as a medicinal product, the broad logic of Regulation No 1768/92 in fact suggests that such a certificate should be granted if all the other conditions of application are satisfied. [25]

46. This conclusion applies a fortiori to the examination of the main objectives of the regulation.

B — *The objectives of Regulation No 1768/92*

47. First of all, the objective of the continuing improvement in public health requires

23 — My emphasis.

24 — This analysis is also corroborated in point 29(2) of the explanatory memorandum annexed by the Commission to its proposal for a regulation, in which it states that the proposal does not provide for any exclusions and points out that 'all pharmaceutical research, provided that it leads to a new invention that can be patented ... must be encouraged, without any discrimination, and must be able to be given a supplementary certificate of protection provided that all of the conditions governing the application of the proposal for a regulation are fulfilled'.

25 — In the present case, under Article 3(c) and (d) of Regulation No 1768/92, the combination at issue has never been granted a supplementary protection certificate and authorisation to place Gliadel on the market was first granted, by the German authorities, on 3 August 1999.

sufficient legal protection to be granted to innovations that allow the therapeutic efficacy of active substances to be increased. [26]

48. In my view, it is not sufficient to encourage research and development of new active ingredients to ensure the continuing improvement of health care. Like MIT and the Commission, [27] I consider that research into new applications for existing active ingredients should be promoted by developing auxiliary substances enabling their use or the enhancement of their pharmacological properties for a specific therapeutic indication. As seems to be the case in the main proceedings, this would make it possible not only to envisage new forms of administration better suited to the patient's specific needs [28] and to increase the efficacy of medicinal combinations, but also to ensure greater safety of use by reducing undesirable effects. [29] If no such research were conducted, I believe that many patients would have to make do with treatment that was not optimal.

49. It seems that this applies in particular to the treatment of neurological disorders such as malignant brain tumours. As MIT points out in its observations, [30] the therapies offered for the treatment of brain cancer, such as chemotherapy, are ineffective in so far as active ingredients administered intravenously are not able to pass through the blood-brain barrier. [31] Biopharmaceutical laboratories have therefore researched and developed new techniques for the effective administration of the active ingredient by conveying it beyond that barrier.

50. These techniques include the development of biodegradable matrices such as the polifeprosan at issue in the main proceedings. Even though this excipient does not have any pharmacological properties of its own, it makes it possible not only to increase significantly the intended therapeutic effect of the active ingredient as a result of a new and inventive mode of administration, but also, through its progressive dissolution, to avoid the harmful side-effects associated

26 — See the first and second recitals in the preamble to Regulation No 1768/92.

27 — See MIT's oral observations and point 21 of the Commission's written observations.

28 — As the Board of Appeal of the European Patent Office held in Decision T-290/86 (OJ EPO 1992, 414), the mode of administration may constitute a decisive factor in medical treatment.

29 — See the order for reference, English version, p. 3, and MIT's written observations, p. 5.

30 — See MIT's written observations, p. 5, and its oral observations.

31 — The blood-brain barrier is composed of capillary cells that have a neuroprotective function, closely controlling access to the brain for substances and nutrients essential to its functioning. This barrier thus forms an obstacle to harmful substances, for example infectious germs, preventing them from entering the brain with the blood. However, this protective mechanism also has the disadvantage of preventing medicinal substances, like those used in chemotherapy, from having access to cerebral tissue.

with the intravenous administration of carmustine. [32]

51. Like the Commission, [33] I consider that this combination gives the active ingredient entirely new properties in terms of efficacy and safety of use. Accordingly, it is of little importance for the grant of the certificate, in my view, that the active ingredient has already been known and used for many years in the treatment of malignant glioma, [34] in so far as it did not have pharmaceutical properties of that kind.

52. Whilst it seems to represent a major therapeutic advance in the treatment of brain tumours, [35] it would be regrettable, in my view, if this new method of therapeutic treatment were not protected in the same way as research into active ingredients alone. Since it very clearly forms part of the action plan to combat cancer launched by the Community, [36] it manifestly plays a role in the continuing improvement in public health within the meaning of the first recital in the preamble to Regulation No 1768/92.

53. Secondly, that regulation seeks to grant medicinal products that are the result of long, costly research legal protection that must be both sufficient to allow pharmaceutical undertakings to cover their investments and equivalent to that enjoyed by other technological sectors. [37]

54. Nevertheless, as is clear from the ninth recital in the preamble to the regulation, this legal protection must be proportionate so as not to compromise the fulfilment of a number of competing political, economic and social interests, such as the placing on the market of generic medicinal products.

32 — As I have already pointed out, the order for reference (p. 3 and 4) and MIT's written observations (p. 5) state that carmustine is a highly toxic substance. Its intravenous administration causes the patient painful and harmful side effects. This substance could even have a lethal effect were it administered in a single dose.

33 — See the Commission's written observations, point 18, and its oral observations.

34 — See order for reference, p. 3.

35 — See MIT's oral observations.

36 — Decision No 646/96/EC of the European Parliament and of the Council of 29 March 1996 adopting an action plan to combat cancer within the framework for action in the field of public health (1996 to 2000) (OJ 1996 L 95, p. 9), amended by Decision No 521/2001/EC of the European Parliament and of the Council of 26 February 2001 extending certain programmes of Community action in the field of public health adopted by Decisions No 645/96/EC, No 646/96/EC, No 647/96/EC, No 102/97/EC, No 1400/97/EC and No 1296/1999/EC and amending those Decisions (OJ 2001 L 79, p. 1). Under that programme, among other things the Community calls for research and development activities in connection with the treatment of that disease to be stepped up.

37 — See the second, fourth and eighth recitals in the preamble to Regulation No 1768/92.

55. Consequently, in order to avoid the risk of monopolisation of the market through the grant of supplementary protection to any new medicinal product which has not been the subject of any therapeutic innovation, Regulation No 1768/92 limits the scope of the certificate to the active ingredient or combination of active ingredients contained in a medicinal product only. [38]

56. As the Commission notes in its explanatory memorandum, [39] a large proportion of the medicinal products placed on the market have only few innovative features, or none at all. It is extremely common for a single active ingredient successively to be granted several marketing authorisations every time that there is a minor change affecting its pharmaceutical form, its dose, its composition (different salt or ester) or its indications. For example, aspirin, which is an active ingredient, may now be marketed in powder or tablet form, in soluble or effervescent form or with added vitamins.

57. In these circumstances, it is clear that a supplementary protection certificate cannot be granted every time that the characteristics of a medicinal combination are slightly changed. If that were the case, the grant of supplementary protection would be disproportionate to the value of the invention and would frustrate the objectives pursued by Regulation No 1768/92.

58. Nevertheless, this could not be the situation in the present case. The Court is hearing a case in which the combination at issue represents a major innovation, resulting from long, costly research, which the regulation precisely seeks to protect. [40]

59. Thus, if a product of this kind were not covered by the certificate, the legal protection granted to it would, in my opinion, be insufficient by some margin to allow research laboratories to recover the sums invested in its development and, a fortiori, to make a legitimate profit from their innovation. In the case at issue, MIT would enjoy only eight years of exclusivity, [41] a term of protection much shorter than that enjoyed in other technological sectors.

38 — A medicinal product is generally composed of one or more active ingredients, excipients and the constituents of the outer covering of the medicinal products (see Annex I, Part 2(A)(1)(1.1) of Directive 2001/83).

39 — See points 11 and 24(2) of the Commission's explanatory memorandum.

40 — Under the second recital in the preamble to Regulation No 1768/92,'... *medicinal products, especially those that are the result of long, costly research* [my emphasis] will not continue to be developed in the Community and in Europe unless they are covered by favourable rules that provide for sufficient protection to encourage such research'.

41 — It can be seen from the order for reference, English version (p. 2), that the application for the basic patent was lodged on 29 July 1987 (that patent will expire on 29 July 2007), and that the authorisation to place Ghadel on the market was granted in Germany on 3 August 1999.

60. In my opinion, such a situation would be liable to discourage research centres located in the Member States from investing in the development of medicinal combinations like the one at issue in the main proceedings, even though such research is essential to the progress of treatment and to the competitiveness of the Community pharmaceutical industry. [42]

61. In the light of these arguments, I therefore take the view that the concept of 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Regulation No 1768/92 must also cover combinations like the one at issue in this case.

62. More specifically, I believe that where the effective treatment of certain illnesses requires an active ingredient to be combined with a substance which, whilst not having any pharmacological properties of its own, allows the biologically active substance effectively to release its therapeutic effects, such a combination must fall within the scope of 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Regulation No 1768/92. It is therefore the necessity of the excipient for ensuring the therapeutic efficacy of the active ingredient that must be the determining factor in ascertaining whether a combination of these two substances is covered by 'combination of active ingredients of a medicinal product'.

63. At the hearing the French Government underlined the difficulties that would be faced by the national bodies responsible for granting the certificate [43] in applying such a criterion. It expressed its concern inter alia over the risk of different practices emerging in each Member State.

64. In my view this concern, however legitimate, does not call my analysis into question.

65. First of all, I do not think that the application of this criterion, which is common to all the Member States, will give rise to particular difficulties.

66. I believe that the national bodies have the necessary information in sufficient quantity to apply this criterion. The grant of a supplementary protection certificate requires an examination not only of the basic patent,

42 — As the Commission notes in paragraph 6 of its explanatory memorandum, since the 1980s there has been a constant fall in the number of molecules of European origin that have reached the research and development stage, whilst there has been a steady rise in the market shares of pharmaceutical laboratories located in the United States and in Japan because of a more innovation-friendly environment.

43 — 'National bodies'.

but also of the marketing authorisation.[44] Thus, the description contained in the basic patent makes it possible to disclose the invention claimed and the advantageous effects of the invention with reference to the background art.[45] The marketing authorisation must contain information with a high level of precision on the characteristics of the medicinal product and its constituents, and on its pharmaceutical qualities and its therapeutic efficacy.[46]

67. Secondly, even though there is a risk that the national bodies will adopt different assessments in applying this criterion, I consider that that risk is inherent in the procedure for the grant of the certificate itself. Although Regulation No 1768/92 seeks to establish uniform conditions for obtaining a certificate in all the Member States,[47] the grant of the certificate remains a national procedure.[48] As is the case with the grant of a national patent, it is inevitable that the national bodies are involved in the assessment and, in my view, the grant of a protection right at national level continues to be imprinted with the legal traditions of each State.[49]

68. In the light of all these arguments, I suggest that the Court answer the questions referred for a preliminary ruling to the effect that the concept of 'combination of active ingredients of a medicinal product' within the meaning of Article 1(b) of Regulation No 1768/92 must be interpreted as not precluding the grant of a supplementary protection certificate to a combination of two substances, one of which is a known substance with pharmacological properties of its own for a specific therapeutic indication and the other is necessary for the therapeutic efficacy of the first substance, for this indication.

44 — See Article 8(1) of Regulation No 1768/92.

45 — Under Rule 27(1) of the Implementing Regulations for the Munich Convention, the description contained in the basic patent must specify the technical field to which the invention relates and the background art. It must also disclose the invention, as claimed, in such terms that the technical problem can be understood, and state any advantageous effects of the invention with reference to the background art. Lastly, it must describe in detail at least one way of carrying out the invention claimed and indicate explicitly the way in which the invention is capable of exploitation in industry.

46 — See Article 6 et seq. of Directive 2001/83.

47 — See the seventh recital in the preamble to Regulation No 1768/92.

48 — See Article 9(1) of Regulation No 1768/92.

49 — The Enlarged Board of Appeal of the European Patent Office held in a decision of 11 December 1989 in Case G2/88 Mobil Oil III (G-2/88, OJ EPO 1990, p. 93) that the determination of the protection conferred by a national patent has for a long time varied according to the national philosophies of each State. Despite the entry into force of the Munich Convention, a Protocol on the Interpretation of Article 69 of the Convention, which concerns the extent of the protection conferred by a European patent, was adopted in order to prevent differences of assessment between the Contracting States from developing. However, even today, there are major disparities between the national rules, as is shown by the adoption of Directive 2004/48/EC of the European Parliament and of the Council of 29 April 2004 on the enforcement of intellectual property rights (OJ 2004 L 157, p. 45) (see seventh and eighth recitals).

V — Conclusion

69. In the light of the above considerations, I suggest that the Court answer the questions referred by the Bundesgerichtshof as follows:

'The concept of "combination of active ingredients of a medicinal product" within the meaning of Article 1(b) of Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products must be interpreted as meaning that it does not preclude the grant of a supplementary protection certificate to a combination of two substances, one of which is a known substance with pharmacological properties of its own for a specific therapeutic indication and the other is necessary for the therapeutic efficacy of the first substance, for this indication.'