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**D E C I S I O N**  
**of 30 September 2003**

**Case Number:** T 0785/97 - 3.3.4  
**Application Number:** 89910878.1  
**Publication Number:** 0386229  
**IPC:** C07H 21/00  
**Language of the proceedings:** EN

**Title of invention:**  
SUPPORT-BOUND OLIGONUCLEOTIDES

**Patentee:**  
OXFORD GENE TECHNOLOGY LIMITED

**Opponent:**  
Affymetrix, Inc.

**Headword:**  
Support bound oligonucleotides/OXFORD GENE TECHNOLOGY

**Relevant legal provisions:**  
EPC Art. 54, 56, 87-89, 114, 123(2)(3)

**Keyword:**  
"Late-filed documents - admitted into proceedings"  
"Extension of scope of protection - all requests - (no)"  
"Extension beyond the application as filed - main request and  
second auxiliary request - (yes)"  
"Right to priority - all requests - (no)"  
"Inventive step - first auxiliary request - (no)"

**Decisions cited:**  
G 0004/93, G 0008/93, G 0002/98, T 0156/84, T 0017/86,  
T 0383/88, T 0583/93, T 1016/93, T 0028/94, T 0113/96,  
T 0548/97, T 0633/97

**Catchword:**  
-



Case Number: T 0785/97 - 3.3.4

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.4  
of 30 September 2003

**Appellant I:** OXFORD GENE TECHNOLOGY LIMITED  
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**Decision under appeal:** Interlocutory decision of the Opposition  
Division of the European Patent Office dated  
12 May 1997 concerning maintenance of European  
patent No. 0386229 in amended form.

**Composition of the Board:**

**Chairman:** U. M. Kinkeldey  
**Members:** A. L. L. Marie  
V. Di Cerbo

## Summary of Facts and Submissions

I. European Patent EP 0 386 229, filed on 21 September 1989 and claiming priority from GB 8822228 (21 September 1988), was granted on the basis of a set of 13 claims, claim 1 of which read:

"1. A method of making a derivatised support suitable for oligo-nucleotide synthesis, which method comprises attaching a nucleoside reagent to a support carrying hydroxyl groups by a covalent phosphodiester link which is stable to conditions used for removing protective groups from oligonucleotide chains."

II. An opposition was filed based on Article 100(a) EPC for lack of novelty (Article 54 EPC) and inventive step (Article 56 EPC).

III. The opposition division maintained the patent in amended form pursuant to Article 102(3) EPC on the basis of claims 1 to 7 of auxiliary request 3 (set E), claim 1 of which read:

"1. A method of making a derivatised support suitable for oligonucleotide synthesis, which method comprises attaching a nucleoside 3'-phosphite reagent to a support carrying hydroxyl groups by a covalent phosphodiester link which is stable to conditions used for removing protective groups from oligonucleotide chains, characterised in that the hydroxyl groups are aliphatic hydroxyl groups in which the aliphatic moiety is hexaethoxy."

- IV. Appeals were lodged against the decision of the opposition division by both the patentee (appellant I) and the opponent (appellant II).
- V. With the statement of grounds of appeal (letter of 22 September 1997), appellant II submitted three documents (documents (11) to (13)) and a fourth one (document (14)) with his letter of 12 October 1998.
- VI. Appellant II in his letter of 8 May 2001 withdrew his opposition.
- VII. The Board sent on 5 September 2002 a detailed communication pursuant to Article 11(2) of the rules of procedure of the boards of appeal raising various questions on Articles 87, 54, 56 and 123 EPC and oral proceedings were scheduled on 12 November 2002.
- VIII. Appellant I, in his letter of 20 September 2002, withdrew his request for oral proceedings, submitted a new main request and new auxiliary requests I to III and requested that the Board proceeds directly to a written decision. Claim 1 of the main request read as follows:
- "1. A method of making a derivatised support suitable for oligonucleotide synthesis, which method comprises attaching a nucleoside reagent to a support carrying hydroxyl groups by a covalent phosphodiester link which is stable to conditions used for removing protective groups from

oligonucleotide chains, characterised in that the hydroxyl groups are aliphatic groups in which the aliphatic moiety is alkoxy or polyalkoxy."

Auxiliary request I, with 8 claims, differed from the main request by the replacement in independent claims 1, 2 and 7 of "alkoxy or polyalkoxy" by "hexaethoxy".

Auxiliary request II, with 7 claims, differed from the main request by the replacement of "nucleoside reagent" by "nucleoside 3'-phosphite". Auxiliary request III was the set of claims maintained by the opposition division (cf supra section III).

IX. With the communication of 16 October 2002, the Board cancelled the oral proceedings.

X. The following documents are mentioned in the present decision:

- (1) WO 85/01051
- (5) EP-0 174 879
- (6) S. Pochet et al., Tetrahedron, 1987, Vol. 43, No. 15, pages 3481 to 3490
- (8) R.Schwyzer et al., Helvetica Chimica Acta, 1984, Vol. 67, pages 1316 to 1327
- (9) E. Felder et al., Tetrahedron Letters, 1984, Vol. 25, No. 36, pages 3967 to 3970

(10) EP-0 305 929

(11) U. Maskos and E.M. Southern, *Nucleic Acids Research*, 1992, Vol. 20, No. 7, pages 1679 to 1684

(12) EP-0 292 128

(13) EP-0 235 726

(14) M.S. Shchepinov et al., *Nucleic Acids Research*, 1997, Vol. 25, No. 6, pages 1155 to 1161

XI. As far as they still apply to the present main request and auxiliary requests I to III, the arguments of appellant II can be summarized as follows:

*Article 123(2) EPC*

- although document (11) showed that the derivatisation of the support was a two-step process, comprising a first step of grafting silane groups onto the support and a second step of derivatizing the silane groups with hexaethoxy groups, claim 1 of auxiliary request I, by using the term "hexaethoxy", only made reference to the second step of this derivatisation process. According to decision T 17/86 (EPO OJ 1989, 297, Corr. EPO OJ 1989, 415), when a feature was described in combination with other features and subsequently sought to be claimed separately from them, it had to be evident beyond any doubt to a skilled person reading the original description

that said isolated feature was able to achieve its purpose when isolated from the other features.

- the mention in the claims of the main request and auxiliary request II that the aliphatic moiety of the aliphatic hydroxyl groups was "alkoxy or polyalkoxy" was an unallowable generalisation over the teaching of the application as filed only disclosing the use of hexaethoxy as an aliphatic group. Reference was made to decision T 383/88 (1 December 1991).

*Articles 87 to 89 EPC*

- the disclosure of the priority document was restricted to nucleoside 3'-phosphite reagents.

*Article 54 EPC*

- document (10) in Example 8 disclosed a structure for binding an oligonucleotide onto a support of the general formula P-X-Y-N-Z-S, in which S was the oligonucleotide, P-X the support and Y-N-Z a linker which differed from the support of the patent in suit by the nature of component Y. However, document (10) on page 5 (lines 22 to 39) listed various possibilities for Y, one of which gave in association with Example 8 the same structure as in the patent in suit.
- the ribonucleoside of document (1) was encompassed by the term "alkoxy or polyalkoxy" used in the claims of the main request and auxiliary request II and Figure 5 of document (1) showed a

structure in which the three substituents could be alkoxy groups.

- "support 13" of document (6) was a desoxyribonucleoside encompassed by the term "alkoxy or polyalkoxy" of the main request and auxiliary request II.

*Article 56 EPC*

- the technical problem as stated in the patent in suit, ie the provision of a linker between a support and an oligonucleotide chain stable to the conditions used during the deprotection steps of solid state oligonucleotide synthesis was already solved by the structures (ribonucleosides) disclosed in documents (1) and (5). Hexaethoxy was also an obvious alternative solution, since it was known from document (11) that the linker had to be made up of the most stable bonds known in organic chemistry, such as carbon-carbon or ether bonds. Furthermore, the use of hexaethoxy linkers with oligonucleotides was known from documents (12) and (13).
- the technical problem underlying the patent in suit was not solved, since the linker containing a hexaethoxy moiety was not completely stable to ammonia as shown by document (11).
- the technical problem was also not solved across its whole range as required by decision T 583/93 (EPO OJ 1996, 496), since the definition of the linker in the patent in suit was broad enough to



cover linkers containing a sub-linker between the support and the hexaethoxy moiety and the nature of this sub-linker was crucial to the stability of the whole linker.

XII. The arguments submitted by appellant I can be summarized as follows:

*Article 114(2) EPC*

- document (10) was submitted by the opponent six days prior to the oral proceedings before the opposition division and, not having a written statement from the opponent in support of document (10), apart from the indication of the passages he intended to refer to, deprived the patentee of his rights under Rule 55(c), 57(3) and 58(3) EPC and led him to mistakenly limit the claims to nucleoside 3'-phosphite. Document (10) should have been disregarded under Article 114(2) EPC.

*Article 123(2) EPC*

- the pre-treatment of the support, which was the first step referred to in document (11) was not part of the linker as shown by document (1) in which the amberlite pre-treated with carbodiimidazole was defined as the support, as were in the patent in suit the glass beads derivatized with glucidoxypopyltrimethoxysilane.
- the application as filed stated that the hydroxyl groups may be part of a polymeric structure, which either constituted the support or was derivatized

onto it and Example 1 disclosed derivatized beads, in which the alkyl hydroxyl moiety was -  $(\text{OCH}_2\text{CH}_2)_6\text{-OH}$ . Hexaethylene glycol was a polymer with polyethoxy group  $-(\text{OCH}_2\text{CH}_2)_n-$  and thus a member of the family of the polyalkoxy groups -  $(\text{O}(\text{CH}_2)_x)_n-$ . Where hexaethylene glycol worked, it was plausible that also other polyethylene glycols worked. Derivatization using polyalkylene glycols resulted in alkoxy or polyalkoxy groups, so that this amendment represented a reasonable generalisation over the specific disclosure of Example 1.

*Articles 87 to 89 EPC*

- the disclosure of the application as filed in respect of the "alkoxy or polyalkoxy"-feature was the same as that of the priority document. Thus, acknowledgement of the fulfilment of the requirements of Article 123(2) EPC implied that the subject-matter of the patent in suit was also directly and unambiguously derivable from the priority document as required by decision G 2/98 (EPO OJ 2001, 413).
  
- the priority document was not limited to nucleoside 3'-phosphite reagents as shown by the sentence on page 3 (lines 21 to 22) which stated that "reagents commonly used in oligonucleotide synthesis may be used here".

*Article 54 EPC*

- document (10) did not disclose a derivatized support in which the aliphatic moiety was alkoxy or polyalkoxy and there was no teaching pointing at a combination of the disclosure of Example 8 with that of page 5, lines 22 to 39.
- the aliphatic alkoxy or polyalkoxy groups of the patent in suit did not include the cyclic linkers of documents (1) and (6).
- document (5) did not mention whether the support was stable to the conditions used for removing the protective groups from oligonucleotide chains.

*Article 56 EPC*

- the requirement for stability was not to be understood in an absolute sense, but relatively to the purpose of the patent in suit, ie to conditions used for removing protective groups from oligonucleotide chains. Document (11) showed that this requirement was satisfied.
- document (10) was only to be considered under Article 54(3) EPC.
- the problem to be solved in view of documents (1), (5), (8), (9) or, if the priority right was not acknowledged, also document (10), was the provision of an alternative derivatized support for oligonucleotide synthesis. No prior art document gave a pointer towards supports with

alkoxy or polyalkoxy groups. Due to the complex interactions involved in oligonucleotide synthesis the skilled person would not have reasonably expected the derivatized support of the patent in suit with the alkoxy or polyalkoxy linkers to give such high yield and hybridisation selectivity. Furthermore, none of these documents described the use of hexaethoxy as aliphatic moiety.

- the use of hexaethoxy groups as linkers was disclosed in documents (12) and (13) in a context different from the oligonucleotide synthesis, so that the skilled person would not have contemplated to combine them with documents related to oligonucleotide synthesis.

XIII. Appellant I requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request or of the claims of auxiliary request I or, failing that, auxiliary request II, all submitted with the letter of 20 September 2002.

## **Reasons for the decision**

### *Procedural matters*

1. Appellant I has in his letter of 20 September 2002 withdrawn his request for oral proceedings and requested that the Board proceeds directly to a written decision on the basis of the new main and auxiliary requests I and II filed with this letter.

2. Appellant II has withdrawn his opposition. According to decision G 8/93 (EPO OJ 1994, 887), this is considered as a withdrawal of his appeal. As a consequence, the sole pending appeal is that of the patentee and the conclusions reached in decision G 4/93 (EPO OJ 1994, 875), according to which the maintenance of the patent as amended in accordance with the interlocutory decision of the opposition division may not be challenged by the Board, apply here. Therefore, the claims of auxiliary request III, which are the claims maintained by the opposition division cannot be challenged.

*Article 114 EPC*

3. The opponent submitted document (10) six days prior to the oral proceedings before the opposition division with his letter of 30 January 1997 and justified this late submission by the fact that the subject of the oral proceedings had changed due to the amendments made by the patentee. Opponent implicitly made thereby reference to the patentee's submission of 24 December 1996 introducing three new sets of claims (sets A to C).
4. Appellant I stated in his grounds of appeal (letter of 10 July 1997) that the admission into the proceedings of the late-filed document (10) without a written reasoned statement in support of this new reference as required by Rule 55c EPC, apart from an indication of the passage to which the opponent intended to refer to during the oral proceedings (page 11, lines 1 to 16 and Scheme IV), had led him to mistakenly limit the claims to nucleoside 3'-phosphite reagents and further

- deprived him of his rights under Rules 55(c), 57(3) and 58(3) EPC.
5. The established Case Law of the Boards of appeal of the European patent Office (4th edition, 2001, pages 324 to 334) shows that one major criterion for the admission of late-filed documents into the proceedings is their relevance. Besides relevance, other criteria may also be taken into consideration, such as a possible abuse of procedure, the character of being contrary to fair and proper procedure, the breach of the principle of good faith, the degree of procedural complication or the complexity of the examination necessitated by the late-filed document.
  6. The opposition division admitted document (10) into the proceedings because of its relevance (page 7, point 2 and pages 10 and 11 of the decision). This attitude was in the Board's view in agreement with the above mentioned case law and, in particular, with decisions T 156/84 (EPO OJ 1988, 372), T 286/94 (22 June 1995) and T 1016/93 (23 March 1995).
  7. Appellant II submitted documents (11) to (13) with his grounds of appeal (letter of 22 September 1997) and document (14) with his letter of 12 October 1998. Appellant I has not requested the Board to disregard these documents under Article 114(2) EPC and has commented on documents (11) to (13) in his letter of 2 April 1998. The Board, following the conclusions of decision T 633/97 (19 August 2000) considers that the admissibility of the late-filed documents (11) to (14) into the proceedings is not in conflict with the requirements of Article 114(2) EPC, since it does not

hinder the appeal proceedings to be conducted in an effective manner. Furthermore, these documents have been submitted in answer to the decision of the opposition division or to arguments of appellant I and are to be seen with arguments and evidence already on file, which they aim at rendering more convincing. This is the normal behaviour of a party adversely affected by the decision of the first instance (decision T 113/96 (19 December 1997), point 11) or even its right and a duty (T 548/97 (20 February 2001), point 1).

*Article 123(3) EPC*

*All requests*

8. The terms "hexaethoxy" and "alkoxy or polyalkoxy" are more specific than the expression "...carrying hydroxyl groups" used in the claims as granted, of which they are a more restricted embodiment. Therefore, the claims of the main request and auxiliary request II, which mention the term "alkoxy or polyalkoxy" and those of auxiliary request I, which mention the term "hexaethoxy", are more restricted in their scope of protection than the claims as granted.
  
9. The claims of the main request and auxiliary requests I and II being directed to "nucleoside reagent" and "nucleoside 3'-phosphite reagent" have a scope of protection which is either identical to or more restricted than that of the claims as granted which mentioned the general expression "nucleoside reagent".

10. Therefore, the claims of the main request and auxiliary requests I and II fulfil the requirements of Article 123(3) EPC.

*Article 123(2) EPC*

*Main request and auxiliary request II*

11. Example 1 on pages 8 and 9 of the application as filed discloses the derivatisation of ballotini glass beads with hexaethylene glycol. There is no evidence in the application as filed, even if the sentence on page 3 (lines 17 to 20), stating that the hydroxyl groups may be part of a polymeric structure, is taken into consideration, that the teaching of Example 1 can be generalised to the whole family of alkoxy or polyalkoxy molecules. Further, such a generalisation would be in contradiction with the disclosure of document (14)(heading "*Effects of spacer length and charge on hybridisation*" and page 12161, left column), cited as an expert opinion, showing that the nature of the molecule between the support and the oligonucleotide may influence the properties of the support-oligonucleotide complex. Therefore, the claims of the main request and auxiliary request II do not fulfil the requirements of Article 123(2) EPC and are not allowable.

*Auxiliary request I*

12. The subject-matter of the claims of auxiliary request I is restricted to the use of "hexaethoxy" groups as the aliphatic moiety of the aliphatic hydroxyl groups and



finds a basis in the teaching of Example 1 of the application as filed.

13. Appellant II objected that the reference to "hexaethoxy" in claims 1, 2 and 7 of auxiliary request I only stressed the second step of a process which, according to document (11), was a two-step process (page 1680, heading "Linker synthesis") that first involved a condensation of 3-glycidopropyltrimethylsilane to the solid support bearing "silanol" groups and then a cleavage of the epoxide group with a diol, such as hexaethylene glycol. Citing decision T 17/86 (cf supra, section IX), stating that, when a feature was described in combination with other features for the achievement of a purpose, but claimed separately from them, the requirements of Article 123(2) EPC were only met, if it was evident beyond any doubt that said isolated feature was able to achieve its purpose when isolated from the other features, appellant II doubted that this condition was fulfilled by the claims of auxiliary request I.
  
14. The application as filed mentions on page 3, lines 4 to 20 that the nature of the support is not critical to the invention and the only essential feature is that it carries hydroxyl groups in a form accessible to nucleoside reagents and, hence, suggests that the properties of the derivatized support are due to the primer/linker carrying the hydroxyl groups and not to the support produced in the first step of the process. This is reflected by the formulation of the claims of auxiliary request I.

15. A similar teaching on the importance of the primer for the overall properties of a derivatized support for oligonucleotide synthesis can be found in document (1), which discloses in Example 1 the two-step preparation of such a support, in which the first step is the derivatisation of amberlite with carbodiimidazole to introduce reactive groups for the primer (5'-dimethoxytrityl-N<sup>6</sup>-(12-aminododecylamine)-adenosine) and the second step is the reaction with said primer. Document (1) states (page 2, lines 29 to 31; bridging paragraph between pages 10 and 11) that the support system comprises a "polymeric support" and a "primer". The "primer" is (5'-dimethoxytrityl-N<sup>6</sup>-(12-aminododecylamine)-adenosine) and the "polymeric support" is the amberlite derivatized with carbodiimidazole, ie the product of the first step of the process. Document (1) puts the accent on the primer, since it states in the passage from page 2, line 29 to page 4, line 11 of document (1), that in a derivatized support suitable for oligonucleotide synthesis the essential element is the primer. From this statement, the skilled person deduces that the properties of the derivatized support are due to the primer and not to the support produced in the first step of the process.
16. Appellant II has further not provided evidence showing that it was erroneous to consider, as do the patent in suit and document (1), that the properties of the derivatized support are due to the primer, although the burden of proof laid on him. Therefore, the Board, as found in decision T 17/86 (cf *supra*, section XI), is convinced that the properties of the claimed derivatized support are due to the hexaethoxy groups.

17. The subject-matter of the claims of the auxiliary request I relates to the use of "nucleoside phosphite" and reflects the teaching of the application as filed which mentions in the paragraph between page 5, line 1 and page 7, line 15, the use of both nucleoside 3'-phosphite and nucleoside 5'-phosphite. The carbon atom on which the phosphite group is attached is thus no longer relevant and the reference to it can be omitted.
18. Therefore, the claims of auxiliary request I fulfil the requirements of Article 123(2) EPC.

*Articles 87 to 89 EPC*

19. Articles 87 to 89 EPC govern the right to priority and state that a European patent application is only entitled to priority from a previous application in respect of the same invention as was disclosed in said previous application. Opinion G 2/98 (cf supra, paragraph X) rules that the concept of "same invention" should be given a narrow interpretation.
20. The priority document only mentions "nucleoside 3'-phosphite reagent" as attached through the phosphite group to the support. The sentence on page 3 (lines 21 to 22), mentioned by appellant I, stating that "*...Reagents commonly used in oligonucleotide synthesis may be used here...*", which according to appellant I should include nucleoside reagents other than 3'-phosphite ones, follows a sentence (lines 20 to 21) indicating that the nature of the nucleoside 3'-phosphite reagent is not critical and is placed before a sentence referring to a preferred embodiment represented by phosphoramidite, ie a 3'-phosphite

reagent. This sentence is thus embedded in a "3'-phosphite" context and cannot be interpreted in the Board's opinion as extending said context to other nucleoside reagents. On the contrary, these three sentences as a whole teach that any (but only a) nucleoside 3'-phosphite reagent can be used. Therefore, the Board is convinced that, in the light of the conclusion drawn in decision G 2/98 (cf supra), according to which the right to priority has to be examined in a narrow or strict way, a generalisation from the sole disclosure in the priority document of "nucleoside 3'-phosphite" to "nucleoside reagent" is not allowable. Thus, the right to priority under Article 89 EPC cannot be acknowledged for this feature of the claims of auxiliary request I. Therefore, the relevant date for the determination of the prior art in the sense of Article 54(2) EPC is the filing date of the patent in suit, ie 21 September 1989.

21. The consequence thereof is that document (10) which has been published before that date, namely on 8 March 1989, is a prior art document in the sense of Article 54(2) EPC and has to be considered also under Article 56 EPC.

*Article 54 EPC*

22. Document (10), concerned with the preparation of support for oligonucleotide synthesis, describes in Example 8 the preparation of a polypropylene membrane grafted with polyethoxyethylacrylate and treated with O-dimethoxytrityl aminoethanol in presence of DMF. This process does not result in a structure containing hexaethoxy groups as the aliphatic moiety of aliphatic hydroxyl groups as required by the claims of auxiliary

- request I. This holds also true even when Example 8 is seen in relation with the disclosure on page 5, lines 22 to 39, showing a variety of functional groups which can be used to bind the spacer to the support and the first nucleotide, since none of these structures corresponds to a hexaethoxy group.
23. In document (1), the use of a ribonucleoside in the preparation of a support for oligonucleotide synthesis represents a teaching different from that of, and even excluded from, the claims of auxiliary request I, because of the reference to the aliphatic nature of the hydroxyl groups. The same applies to the solution proposed on Figures 5 and 6 of document (1), in which substituents  $R_1$ ,  $R_2$  and  $R_3$  or  $R_3$  and  $R_4$ , respectively, can be alkoxy groups, because document (1) does not explicitly teach the use of hexaethoxy groups as alkoxy groups, which thus is a specific selection of one out of many possibilities covered by this generic term and can establish novelty under the case law of the boards of appeal on selection inventions.
24. In documents (5) and (6) the link between the support and the oligonucleotide is made through the base, which is a disclosure different from that of the claims of auxiliary request I.
25. Therefore, there is no prior art document on file which discloses the method of claim 1 of auxiliary request I. Since independent claims 2 and 7 mention the same characterizing features as claim 1 and claims 3 to 6 and 8 depend on claims 1, 2 and/or 7, the claims of auxiliary request I fulfil the requirements of Article 54 EPC.

*Article 56 EPC*

26. The closest prior art is defined in the Case Law of the Boards of Appeal of the European Patent Office (4th edition, 2001, pages 102 to 106) as a document disclosing a subject-matter for the same purpose or aiming at the same objective and which requires the minimum of structural and functional modifications.
27. Document (1) refers to ribonucleoside as a preferred primer or to structures containing alkoxy groups as substituents, such as those mentioned in Figures 5 and 6, but there is no pointer at hexaethoxy groups and, in Figures 5 and 6, the alkoxy substituents do not bind the nucleoside.
28. In document (5) the oligonucleotide is bound to the support by the base, which is a teaching different from that of the claims of auxiliary request I.
29. Documents (8) and (9) refer to linkers called "CAMET" and "CASET" which not even have an alkoxy structure and do not suggest the use of alkoxy or even hexaethoxy groups.
30. In the Board's opinion, the closest prior art is represented by document (10) which describes a method for preparing a membrane for peptide and/or oligonucleotide synthesis. Example 8 deals with the successful synthesis of an oligonucleotide on a polypropylene membrane grafted with polyethoxyethyl acrylate. The binding of the nucleotide is made by a phosphodiester link with the hydroxyl function of the

ethoxyethyl groups. From the success of the synthesis of an oligonucleotide, it can be deduced that the covalent phosphodiester link between the hydroxyl groups of the ethoxyethyl groups and the oligonucleotide was stable to the conditions used from removing the protective groups from the oligonucleotide chains. Hexaethoxy is not specifically suggested.

31. In view of document (10), the technical problem to be solved can be defined as the provision of an alternative method for making a support for oligonucleotide synthesis.
32. The solution proposed in claim 1 of auxiliary request I is a method using a support carrying hydroxyl groups in which the aliphatic moiety is hexaethoxy. The examples of the patent in suit show that the invention has been successfully performed.
33. For the assessment of inventive step, the question to be answered is whether the skilled person would have been led in an obvious manner to this solution by the disclosure of document (10) considered alone or in conjunction with the common general knowledge or any other prior art documents on file.
34. The patent in suit states on page 2, lines 43 to 46 that the nature of the support is not critical to the invention and has to fulfil a single requirement: it should carry aliphatic hydroxyl groups in a form accessible for reaction with the nucleoside reagent. The expression "*accessible for reaction*" is a warning for the skilled person about the possible occurrence of steric hindrance problems and implies that the linker

- between the support and the nucleoside reagent should not be too short a molecule. The successful performance of the invention as shown in the examples of the patent in suit shows that the hexaethoxy molecule satisfies this requirement.
35. Document (10) does not suggest by itself the use of hexaethoxy groups. However, it is also concerned with the problem of minimizing problems due to steric hindrance and suggests on page 4 (lines 1 to 6) the use of a suitable spacer placed between the support and the first anchored building block. In Example 8, the use of polyethoxyethyl groups, ie alkoxy groups, allows the skilled person to avoid these problems. These polyethoxyethyl groups are representative of a family of molecules satisfying the conditions for avoiding steric hindrance problems, of which the hexaethoxy molecule of the patent in suit is another member.
36. The hexaethoxy molecule of the patent in suit does not present advantages over the polyethoxyethyl one of document (10), since both molecules allow the skilled person to avoid steric hindrance problems and are stable to the conditions used for removing protective groups from oligonucleotide chains. Therefore, the hexaethoxy molecule is an obvious alternative to the polyethoxyethyl molecule used in document (10).
37. The use of the hexaethoxy molecule as a spacer to avoid steric hindrance problems is disclosed in document (12), which is concerned with the detection of DNA probes labelled with reporter groups of huge size, such as avidin or antibodies (page 8, lines 39 to 49).



38. The detection of DNA probes using reporter molecules is a technical domain different from, but close to that of solid-phase oligonucleotide synthesis, since both domains concern the interaction of DNA sequences with other molecules (support or reporter groups) and are thus facing similar problems, such as those caused by steric hindrance. The combination of the teaching of documents (10) and (12) is thus straightforward and leads the skilled person to consider the hexaethoxy group as the group of choice to be used as a linker between support and oligonucleotide for solving problems related to steric hindrance. The Board is thus convinced that the subject-matter of the claims of auxiliary request I is obvious for the skilled person in view of the combination of documents (10) and (12) and does not fulfil the requirements of Article 56 EPC.

## **Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairwoman:

P. Cremona

U. Kinkeldey