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D E C I S I O N
of 30 September 1998

Case Number: T 0145/95 - 3.3.4

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Language of the proceedings: EN

Title of invention:
Newcastle disease virus gene clones

Patentee:
British Technology Group Limited

Opponent:
Akzo Nobel Pharma B.V.

Headword:
Newcastle disease virus/BTG

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step (no)"

Decisions cited:
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Boards of Appeal

Chambres de recours

Case Number: T 0145/95 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 30 September 1998

Appellant: British Technology Group Limited
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London EC4M 7SB (GB)

Representative: Percy, Richard Keith
Patents Department
British Technology Group Ltd
10 Fleet Place
London EC4M 7SB (GB)

Respondent: Akzo Nobel Pharma B.V.
(Opponent) Wethouder van Eschstraat 1
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 28 December 1994
revoking European patent No. 0 227 414 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: L. Galligani
R. E. Teschemacher

Summary of Facts and Submissions

- I. The appeal lies from the decision of the opposition division issued on 28 December 1994 whereby the European patent EP-B-0 227 414, which had been opposed under the terms of Article 100(a) and (b) EPC by one party, was revoked under Article 102(1) EPC. The earliest priority date of the patent was 18 December 1985.
- II. Basis of the decision were the claims as granted in the two versions for Spain (ES) and for the other contracting states (non-ES) (main request) and, as an auxiliary request, the same sets of claims with the deletion of claim 6 for ES and claim 7 for non-ES states.

Claim 1 as granted (non-ES states) read as follows:

"1. DNA comprising (1) a nucleotide sequence encoding an F or HN polypeptide of Newcastle Disease Virus Beaudette C strain having the amino acid sequence hereinbefore shown above the nucleotides herein numbered 47-1705 or 1915-3645 respectively; or (2) a nucleotide sequence which has at least 80% nucleotide homology with the nucleotide sequence coding for the F or HN gene of Beaudette C strain numbered 47-1705 or 1915-3645; or (3) a nucleotide sequence which encodes the F₁ or F₂ polypeptide or an epitopic portion of the F or HN polypeptide encoded by a sequence defined in (1) or (2) above."

Claims 2 to 3 related to specific embodiments of the sequence according to claim 1; claims 4 to 7 were directed to a recombinant DNA comprising a DNA sequence

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according to the preceding claims, claim 7 being in particular directed to a recombinant DNA wherein the vector DNA comprised DNA from fowlpox virus; claim 8 was directed to host cells containing recombinant DNA according to claims 4 to 7.

The corresponding claims for ES were formulated in terms of a method.

III. A total of sixty-five citations was taken into account by the opposition division which considered that the subject-matter of the main request as well as that of the auxiliary request lacked an inventive step having regard to the following documents:

- (2) Choppin et al., J.Infect.Dis., 1981, volume 143, 352 to 363;
- (6) Richardson et al., Virology, 1980, volume 105, 205 to 222;
- (37) Poster displayed at a meeting of the Biochemical Society at Oxford, England on 17 July 1985 (sheets A to D);

in combination with the general technical knowledge of the various recombinant DNA techniques for cloning and expressing a viral gene. The use of any of the known techniques would have had a good chance of success.

Furthermore, the opposition division held that the embodiment of claim 7 of the main request was not sufficiently disclosed.

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IV. With the statement of grounds of appeal, the appellants (patentees) filed additional documents (66) to (91). In reply thereto, the respondents (opponents) filed additional documents (92) to (109). Later, the appellants filed additional documents (110) to (127) and the respondents documents (128) and (129).

V. Of the many documents cited by the parties, the following are referred to in the present decision in addition to those already mentioned above in Section III.:

(8) Collins et al., J. Virology, 1982, volume 43, pages 1024 to 1031;

(11) Blumberg et al., Cell, May 1985, volume 41, pages 269 to 278;

(12) Hiebert et al., J. Virology, April 1985, volume 54, pages 1 to 6;

(24) Lathe R. J., J. Mol. Biol., 1985, volume 183, pages 1 to 12;

(38) Schuy et al., Virus Res., 1984, volume 1, pages 415 to 426;

(50) Maniatis et al., Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory, 1982, pages 326 to 328 and 374 to 375;

(107) Cann et al., Nucl. Ac. Res., 1983, volume 11, pages 1267 to 1281.

VI. The board outlined the points to be discussed at oral proceedings in a communication pursuant to article 11 of the rules of procedure of the boards of appeal.

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- VII. With letter dated 14 July 1998, the appellants deleted claim 7 in the set for non-ES states and claim 6 for ES.
- VIII. Oral proceedings took place on 28 July 1998. During oral proceedings a modified request was filed as a sole request in the two versions for non-ES states and ES. It comprised claims 1 to 6 and 8 (renumbered 7) as granted (claims 1 to 5 for ES) with the proviso that the expression "or an epitopic portion of the F or HN polypeptide" was deleted from claim 1 (non-ES states). A corresponding amendment was carried out in claim 1 for ES.
- IX. The appellants submitted in essence the following arguments:
- (a) The respondents had suggested two methods by which the skilled person would have readily identified F & HN cDNAs, namely the "degenerate oligonucleotide probes" and the "long oligonucleotide probe". Only at a later stage they suggested a third approach, namely the "mRNA approach". All the suggested routes were on (or over) the very edge of what was technically reasonable and believable at that time. Moreover, the expert could not afford to try every possibility. The board was invited to take the "real" life situation into account.
 - (b) As regards the "degenerate oligonucleotide approach", this required that the amino acid sequence relied upon be correct and identical in the strain being cloned. In the present case, the uncertainties, inconsistencies and errors in the known partial amino acid sequences of the NDV F and HN proteins (cf documents (38) vs (2)/(6) and (38) vs (37)), the NDV strain variation (see eg the declaration of Dr D. Alexander), the high

degree of degeneration of the probes would have either led the skilled person to failure or rendered his/her task technically extremely difficult, if not impossible.

(c) As regards the "long probe approach", there was no suitable F amino acid sequence known in the art, there was no information about the NDV strain used in document (37), no suitable codon ssRNA viral codon usage tables were available, there were doubts concerning the validity of the "G/T" rule. Under these circumstances, there was no expectation that the skilled person could design with reasonable effort a probe having the required homology. The probe design put forward by the respondents (cf Dr Sondermeijer's experiment), which was made with hindsight, was unable to suggest a suitable probe (lack of perfect homology, non-specific hybridisation). This demonstrated the complexity of the technical situation in real life.

(d) As for the so-called "m-RNA approach", the fact that it was the last resort for the respondents demonstrated that they themselves were not very convinced of its plausibility. The problems with this approach were that it was very labourious and it was unlikely to have been the skilled person's first choice. The skilled person would not have placed much confidence in the "provisional" information given in the "unrefereed" poster because: the authors had not published any work on the cloning of any viral gene; important experimental details of the cloning procedure were missing; the NDV strain used was not disclosed; there were problems in resolving NDV mRNAs, especially the F mRNA, and with the use of ³²P-labelled probes; NDV cDNA libraries were complex.

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(e) Thus, none of the envisageable techniques would have been considered by the skilled person to have had a good chance of success in the case of NDV.

X. The respondents argued essentially that in the period 1980-1985 progress in the biotechnological field went so fast that the techniques based on the long probe or short probe approach had become established and were part of the common general knowledge.

The known amino acid sequence of the 69 amino acids long fragment of the NDV HN protein would have been an appropriate starting point for designing a long probe. The prior art demonstrated that regions comprising even more than one 6-fold degenerate codons could successfully be used for probe design and that the "G/T rule" was a valid tool therefor. Moreover, the guaranteed minimum homology of a probe with the actual sequence was sufficiently high to encourage the skilled person. Dr Sondermeijer in his declaration had demonstrated that this was indeed possible.

The available amino acid sequence information could also be used as an appropriate starting point for designing a mixture of fully degenerated short probes. The fact that similar types of probes had proven successful in much more complex situations would have given enough confidence to the skilled person in this approach.

Furthermore, the disclosure in document (37) of a method of proven practical value for arriving at the DNA sequences encoding the F and HN protein of NDV would have encouraged the skilled person to repeat the experimental steps and determine the nucleotide sequences of the NDV DNA molecules. Document (37) did not report any particular difficulty in the construction of a NDV library from the genomic RNA of

purified virions and in the identification of a set of clones spanning the whole NDV genome, including the F and HN gene. The skilled person had thus a more than reasonable expectation of success in repeating and completing the work of document (37).

XI. The appellants requested that the decision under appeal be set aside and the patent be maintained on the basis of the two sets of claims (for ES and for the other Contacting States) submitted during the oral proceedings (sole request).

The respondents requested that the appeal be dismissed.

XII. At the end of oral proceedings, the Chairwoman pronounced the following:

- 1. The debate is closed.
- 2. The order of the decision will be issued by 30 September 1998.

Reasons for the Decision

- 1. The only issue to be discussed is inventive step as the amendments which characterise the present claims in comparison with the claims as granted did not give rise to any formal objections under Article 123(2)(3) EPC.
- 2. Claim 1 on file covers two main alternative embodiments, namely a DNA encoding an F polypeptide or a DNA encoding a HN polypeptide of Newcastle Disease Virus (NDV) Beaudette C strain. If any one of the two embodiments turns out to lack an inventive step, the claim as a whole fails under Article 56 EPC. The two

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aspects of the claimed invention have to be dealt with separately. The board finds it appropriate to discuss in detail firstly the inventive step of a DNA encoding a HN polypeptide.

3. In the board's judgement, the closest prior art with respect to this embodiment is represented by document (37). This is the copy of a poster made of four sheets (A to D) exhibited at a meeting of the Biochemical Society at Oxford, England on 17 July 1985. As reported in the description of the patent in suit (cf page 4, lines 29 to 37), this poster presentation was accompanied by an oral paper, with overhead projection, which "went no further in content than to the poster" (loc.cit., lines 36 to 37). Nothing in the file proves that this was not the case. The poster, without giving any nucleotide sequence information, reports the results of work in connection with the cloning of the HN and F genes of NDV. In essence, it conveys the following information:

- (a) Object of the work was to clone and sequence full length copies of the viral glycoprotein genes with the eventual aim of producing a hybrid virus vaccine (cf sheet A, "Introduction", second full paragraph);
- (b) The entire HN and F genes of NDV were cloned into pBR322 (cf sheet D, "Summary"). Sequence analysis demonstrated conservation of protein sequence and RNA control sequence between NDV and other paramyxoviruses (loc.cit.). The 69-residue amino acid sequence of the C-terminus of the HN glycoprotein was deduced and compared with the corresponding sequence of the same protein of the

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simian virus 5 (SV5; reference being made in this respect to Hiebert et al., which is document (12) in the present appeal proceedings) (cf sheet C, last paragraph and sheet D, Figure 3);

(c) The results were achieved essentially through the following experimental steps:

- Isolation of genomic RNA from egg-grown NDV by protease treatment, phenol extraction and ethanol precipitation;
- Preparation of cDNA by reverse transcriptase, tailing of RNA:DNA hybrids with oligo dC, annealing to pBR322 cut at the PstI restriction site tailed with oligo dG (reference being made to Cann et al., which is document (107) in the present proceedings);
- Transformation into E. coli and selection on the basis of ampicillin sensitivity / tetracyclin resistance and detection of NDV-specific recombinants by colony hybridisation using ³⁵S labelled cDNA to viral RNA as a probe. Figure 1 shows that upon gridding of 100 tetracycline resistant transformants some clones with NDV-specific inserts were indeed obtained (dark streaks);
- Preparation on a larger scale of large inserts (>1 kb) and mapping to each other by dot blot hybridisation and restriction enzyme mapping. Determination of the portions of the NDV genome contained in the inserts by Northern blot hybridisation, the individual mRNA for this purpose being resolved on agarose-formaldehyde gels and ³²P labelled plasmid DNAs being used as probes. Figure 2 reports the results of the

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Northern blot analysis, in particular in lane 1 the probing with plasmid DNA specific to HN is shown. Figure 3 reports the order of the genes in NDV and the map of the cloned inserts;

- DNA sequence analysis of the C-terminal portion of the HN gene. This revealed an open reading frame in the deduced protein coding region and the sequence 3'AUUCUUUUU 5' downstream from the open reading frame.

4. The appellants argue that the skilled person would not have relied on the disclosure of document (37) because:

- (i) it was an unrefereed publication with a provisional character;
- (ii) none of the authors had published any work on the cloning of any viral gene;
- (iii) the experimental details relating to cloning were non-enabling; and
- (iv) the NDV strain used was not disclosed.

5. The board cannot share this view for the reasons given hereinafter.

In respect of items (i) and (ii), the board observes that, when evaluating inventive step, the skilled person is assumed to be aware of the totality of the prior art pertinent to the relevant area of technology, ie of everything made available to the public by any means (cf Article 54(2) EPC). Document (37) was indeed pertinent to the technical area of NDV gene technology, in particular to the cloning of the NDV glycoprotein genes, and contained information addressed to the person skilled in the art. Thus, he or she would have

taken this disclosure into account when working at the cloning of NDV genes. Whereas the particular reputation of an author may give particular attention and credibility to his or her publication, there is no rule that publications of less known authors are not taken seriously by other scientists. Rather, it is the technical content of a piece of prior art which decides in the first place on its acceptance. Therefore, the fact that the work was not refereed and was authored by scientists who had prior no experience in this specific technical area, are factors which would not have prevented the skilled person from considering document (37) as relevant.

As regards item (iii), the appellants were unable at oral proceedings to point to any misleading or non-enabling information contained in document (37). They merely indicated that the patent in suit contained more experimental details than the poster presentation. This, however, per se does not necessarily mean that the description in document (37) was non-enabling.

As regards item (iv), the fact that the NDV strain used in document (37) was not mentioned did not diminish the validity of the report. As nothing therein indicated that the results were linked to the peculiarities of a given strain, the skilled person had no reasons to doubt that the disclosed experimental approach would be applicable to any strain of NDV, including the known Beaudette C strain. At oral proceedings, both parties agreed that there were no prejudices against using the latter strain for cloning work.

- 6. Thus, in the board's view, the disclosure of document (37) is a suitable starting point for an analysis of inventive step.

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7. In the light of document (37), the problem to be solved was the identification and cloning of a full length DNA segment encoding a HN polypeptide of NDV. The solution provided by the patent in suit is the DNA sequence referred to in claim 1, item (1) (nucleotides numbered 1915-3645) as well as DNA sequences having at least 80% homology thereto (cf. claim 1, item (2)).

8. In dealing with this question, both parties have engaged in intense discussions about the strategy that the skilled person would have adopted in order to find a solution to the stated problem, emphasis being put especially on the so-called "mixed oligo probe" and "long nucleotide probe" approaches (cf Sections IX and X supra). Both these methods rely on the knowledge of the amino acid sequence of the protein encoded by the desired gene. Based thereupon, either a mixture of synthetic single-stranded oligonucleotides, that differ from each other in one single base only, or a single longer "optimal" probe is prepared and used to screen genomic or cDNA libraries for the desired gene. However, due to the redundancy of the genetic code, the design of perfectly matched probes is largely a matter of guesswork and chance (cf eg document 24). Even more so, if only partial amino acid sequence data are available, as in the case at issue.

For the HN polypeptide a 69-residue amino acid sequence at the C-terminus was known from document (37).

The **respondents** submitted that this information would have been sufficient for a skilled person for designing suitable probes which would have readily led to the successful cloning of a DNA encoding a HN polypeptide.

In reply thereto, the appellants argued that factors like inter alia the NDV strain variation, the complexity of the NDV cDNA library, the uncertainties in the amino acid sequences, the high degree of degeneracy would have rendered difficult and complex the research needed to reach the objective. In the appellants' view, neither of the two approaches would have been considered by the skilled person to have had a good chance of success in the case of NDV.

In the appealed decision, the opposition division adopted the opponents-respondents' position.

9. In the board's judgement, the parties, by engaging in a theoretical dispute about the feasibility of the said probe strategies, have lost track of the prior art situation. In fact, the genomic RNA route (improperly referred to throughout the proceedings as the "mRNA approach") was discussed only as a third option. However, in the board's view, having regard to the disclosure of document (37) and to other prior art related to paramyxoviruses, the **first option** of the skilled person would have been indeed a strategy based on the genomic RNA relying on the guidance of document (37). In fact, in view of the good results reported in the latter, the skilled person would have readily repeated and completed its teaching. He or she was aware of the fact that by using this route the guesswork necessary when attempting the alternative "mixed oligo probe" and "long nucleotide probe" strategies, and the possible complications in relation to the NDV strain variations, would have been avoided.
10. The crucial question is thus whether the skilled person, starting from the teaching of document (37) needed more than ordinary skill in order to arrive at the claimed solution.

11. Document (37) outlined the essential experimental steps which had led the authors to the cloning inter alia of the HN gene of NDV (cf point 3c supra). All these steps involved techniques well known in themselves with which the skilled person in 1985 was quite familiar. The skilled person would have expected the repetition of the relatively detailed experimental protocol to involve a certain amount of trial and error, but nothing out of the ordinary. The further data reported in the poster presentation (order of the genes, presence of the sequence 3'AUUCUUUUUU 5' downstream from the open reading frame of the HN gene, the 69-residues amino acid sequence at the C-terminus, the high homology with the corresponding sequence of SV5) would have provided further means for checking the results obtained. All this information would have given the skilled person a reasonable expectation of obtaining clones with overlapping inserts of the NDV genome, in particular clones spanning the HN gene, as achieved by the authors of the poster presentation. The skilled person would have considered the said experimental protocol to be applicable to any strain of NDV, including also the known Beaudette C strain (cf point 5, paragraph dealing with item (iv) supra).

From Figure 3 of the poster presentation, the skilled person was aware of the fact that the cloning work had not been completed because, although partially overlapping inserts for the entire HN and F gene had been cloned into pBR322, none of them was a full length copy of a gene. However, the skilled person knew that, once cloned inserts spanning a gene were available, based on their restriction map, such full length copy of the gene could be obtained without difficulties by ligating together the appropriate restricted DNA

fragments. This step could be done by any of the known ligation techniques depending on the termini carried by the fragments. This is confirmed by the description of the patent in suit on page 7, lines 17 to 26 where reference to "well known methods" is made.

12. Thus, in the board's judgement, when working within the framework provided by the disclosure of document (37), the skilled person did not need more than ordinary skill in order to arrive by known methods at a DNA sequence encoding a HN polypeptide falling within the terms of claim 1. It was merely a matter of filling the gap in information by using common general knowledge and routine skill, this being a task which could be performed by the skilled person.

13. In support of the contention that the skilled person would not have had confidence in the genomic route described in document (37), the appellants submitted essentially that:

(a) it was a very labourious and slow route and thus it would not have been the first choice, also in view of the limited time and resources available to the skilled person. This was confirmed also by the fact that it wasn't even the opponents' first choice in their attack on inventive step.

(b) There were problems in resolving NDV mRNAs, especially the F mRNA, and with the use of ³²P-labelled probes. In fact, prior art document (8) had not demonstrated that NDV mRNAs could be resolved to such an extent that the identity of ³²P-labelled cDNA probes could be established and had also failed to demonstrate that the coding capacity of individual NDV RNA bands had been identified unambiguously.

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(c) The poster presentation contained far less experimental details than the patent in suit. Success was achieved by the appellants by way of an ingenious combination of methods and measures which the skilled person would not have derived from the poster presentation or from common general knowledge. These were, for example, the use during RNA extraction of a special buffer containing vanadyl ribonucleoside and of 8-hydroxyquinoline during phenol extraction, or the measure of simultaneously ligating the restricted DNA fragments in order to make a full length copy of the genes.

14. In the board's view the above arguments are not convincing for the following reasons:

(i) As regards item 13(a), the reasons why the board believes that the skilled person's first choice would have indeed been the genomic route have already been given in point 9 supra. It should also be added that the said route was basically the one chosen for cloning the HN gene of other paramyxoviruses (see documents 11 and 12). This was a further reason for taking it. Moreover, the complexity of the theoretical considerations put forward by the parties in relation to the "mixed oligo probe" and "long nucleotide probe" strategies shows that the genomic route was not more labourious, slow and expensive than the said strategies. The skilled person would in fact have considered the genomic route to be simpler, more straightforward and thus preferable.

(ii) In respect of item 13(b), it is noted that the prior art document (8) had reported the electrophoretic separation of the individual viral mRNAs, each of them containing a single unique major transcript and encoding a single unique polypeptide in a cell-free translation system (cf page 1029, "Discussion"). In particular, it showed that the RNA of band 5 quite distinctly encoded unglycosylated HN. The said document does not contain any statements which could have suggested to the skilled person that the separation of the HN mRNA species represented a problem. Even the description of the patent in suit itself relies on a reference to document (8) when describing the resolution of the individual NDV mRNA (cf page 9, lines 54 to 56). Moreover, the results of the Northern blot analysis of the poster presentation (cf item 3c, 4th paragraph supra) would have confirmed that NDV mRNAs could be resolved to such an extent that the identity of ³²P-labelled cDNA probes could be established.

(iii) As regards item 13(c), it is a fact that there is a difference in the amount of experimental details between the poster presentation and the description of the patent in suit. This is not surprising as poster presentations are usually limited to the essential information and leave aside details about the techniques used, especially when these are well-known. However, having established that the poster presentation did not convey false or misleading information (cf point 5, paragraph concerned with item iii) supra), the relevant question is whether - as submitted by the appellants - the skilled person

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would have had to unduly struggle in order to find the right conditions for successfully carrying out the experimental plan outlined in the said poster.

In respect of this question, it should firstly be noted that the general experimental outline in the patent in suit (cf pages 8 to 11 of the patent in suit) is identical to the one reported in document (37). As a matter of fact, the description emphasizes that the methods and techniques used for preparing the subject DNA were conventional (cf. page 7, lines 6 to 11, 17 to 26). However, on lines 11 to 16 of the same page it is stated: "The ingenuity of the method employed lies really in the mapping technique and overcoming the difficulty that it was not possible unambiguously to hybridise sub-clones of recombinant DNA to RNA of the F genes. The NP and F genes have very similar relative molecular masses, making it difficult to perform an adequate separation of their mRNA by electrophoresis. By ingenious combination of various methods, however, it was possible unambiguously to assign the various clones to the correct genes." (page 7, lines 11 to 16).

In respect of the latter statement, the following is observed:

(a) As regards the alleged difficulties in the mapping techniques, it cannot be seen where they could have lay, because, for the reasons already given in points 11 and 12 supra, the repetition of the work in document (37) would only have required a feasible amount of experimentation in

an area already explored. This did not involve undue burden or the need to apply skill out of the ordinary at the priority date 1985.

(b) As regards the alleged difficulties in hybridising sub-clones of recombinant DNA to RNA, it is noted that these admittedly related to the F or NP genes which are not under discussion here.

(c) As for the allegedly ingenious measures which at oral proceedings were presented as paramount for achieving cloning, nothing in the description of the patent in suit nor in the file supports this contention by the appellants which was rebutted by the respondents. The board cannot see why the skilled person would have expected the RNA extraction or the ligation of restricted fragments to be potential sources of difficulties, especially in the light of the state of the art in 1985. The skilled person knew that during the extraction and purification of the genomic RNA it was necessary to minimize the activity of RNAases, especially when full length cDNA were aimed at. The addition of RNAases inhibitors was a known option, vanadyl-ribonucleoside complexes being a well-known potent inhibitor (cf the widely used textbook by Maniatis et al., 1982, page 213; cf document (50)). That the latter complexes were removed from RNA by extraction with phenol containing 8-hydroxyquinoline was also well known (ibidem, page 188).

(d) As regards the ligation step, it is noted that the description of the patent in suit on page 7, lines 17 to 26 indicates that, in order to produce full length or nearly full length

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genes, appropriate portions of DNA inserts are ligated together using "well known methods" (loc.cit. line 20 as well as line 23). This passage refers in particular to sequential ligation of the appropriate inserts depending on the termini and on the restriction enzyme used. The protocols in respect of the preparation of full length cDNA encoding the F and HN polypeptide report then a simultaneous ligation step (cf page 18, line 31) without pointing to any difficulties encountered when using a different scheme. In the board's judgement, the ligation step was not an insurmountable step in the cloning procedure for which particular measures had to be taken. The skilled person would not have thought of ligation as being a particularly difficult step in the construction of full length cDNA fragments encoding HN polypeptide. Sequential or simultaneous ligation methods, both belonging to common general knowledge in 1985 and both involving only routine trials, were within his or her design freedom with an equal chance of success.

Thus, in the board' judgement, the skilled person would not have had to unduly struggle in order to repeat and complete the work described in document (37) (see also point 12 supra).

15. For these reasons, an inventive step is to be ruled out in respect of the aspect of the claimed invention concerned with a DNA encoding a HN polypeptide. Consequently, claim 1 of the main request which covers inter alia this embodiment lacks an inventive step as a whole.

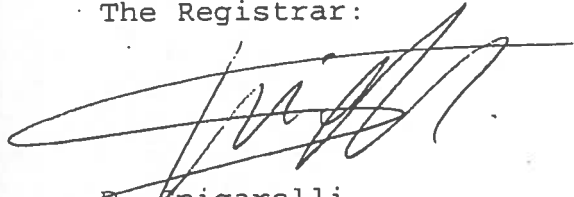
16. As no separate request has been filed covering only the embodiment related to a DNA encoding an F polypeptide, there is no need to deal with the question whether this particular aspect of the claimed invention involves an inventive step.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:



D. Spigarelli

The Chairwoman:



U. M. Kinkeldey



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