The opinion in support of the decision being entered today was not written for publication
and is not precedent of the Board.

Paper No. 62

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte WOLFGANG LUDWIG, KARL-HEINZ SCHLEIFER,
CHRISTOPH KESSLER, RUEDIGER RUEGER
and ANNE STERN

Appeal No. 1997-0160
Application No. 08/073,985[1]

ON BRIEF

Before WINTERS , WILLIAM F. SMITH, and SPIEGEL, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner finally rejecting claims 2, 4, 6 through 12 and 14 through 24 and refusing to allow claims 5 and 13 as amended subsequent to the final rejection,[2] which are all of the claims pending in this application. Claim 1 is illustrative and reads as follows:

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[1] Application for patent filed June 8, 1993. According to appellants, this application is a continuation of application 07/772,026 filed October 8, 1991, now abandoned.

[2] The amendments filed December 14, 1995 (Paper No. 42) and March 22, 1996 (Paper No. 49) amending claims 5 and 13 were entered by the examiner in the advisory actions mailed April 26, 1996 (Paper No. 43) and May 6, 1996 (Paper No. 51).

13. A method for genus-specific and species-specific detection of bacteria in a sample liquid, comprising the steps of:

hybridizing RNA of target bacteria with a primer which is complementary to a genus-specific region of RNA of said target bacteria, wherein the 3' end of said primer is only complementary to the RNA of said target bacteria and not complementary to the RNA of other bacteria in said sample which differ from the genus of said target bacteria;

elongating said primer in the presence of a suitable polymerase and the four deoxyribonucleotides to form an elongation product;

labeling said elongation product concurrently with the elongation of said elongation product or subsequent to said elongation;

hybridizing said elongation product with a species-specific labeled oligonucleotide after denaturation to form a hybridization elongation product; and

detecting said hybridization elongation product.

The references relied on by the examiner are:

Mullis et al. (Mullis)	4,683,195	Jul. 28, 1987
WIPO Int. App. (Hogan)	88/03957	Jun. 2, 1988

Frohman et al. (Frohman), "Rapid production of full-length cDNAs from rare transcripts: Amplification using a single gene-specific oligonucleotide primer," Proceedings of the National Academy of Sciences, USA, Vol. 85, pp. 8998-9002 (December 1988).

Appellants rely on the following references in their brief (pages 13 and 18):

WIPO Int. App. (Hogan and Kohne)[3]	84/02721	Jul. 19, 1984

[3] Hogan and Kohne was made of record in the Information Disclosure Statement filed July 12, 1995 (Paper No. 38) by appellants.

LISTERIA, LISTERIOSIS AND FOOD SAFETY by Elliot T. Ryser (Ryser), pp. 217-39 (Marcel Dekker, Inc., New York) (1991).[4]

ISSUE[5]

Claims 2 and 4 through 24 stand rejected under 35 U.S.C. § 103 as being unpatentable over Mullis in view of Hogan and Frohman. We REVERSE.

In reaching our decision in this appeal we have given careful consideration to the appellants' specification and claims and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's answer (Paper No. 52, mailed June 11, 1996) for the examiner's reasoning in support of the rejection and to the appellants' brief (Paper No. 50, filed March 22, 1996) for the appellants' arguments thereagainst.[6]

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[4] Ryser was submitted as an attachment to appellants' "SUPPLEMENTAL RESPONSE AFTER FINAL REJECTION" filed September 9, 1994 (Paper No. 30).

[5] In the advisory action mailed April 26, 1996 (Paper No. 43), the examiner stated that the amendment filed December 14, 1995 (Paper No. 42) overcame the final rejection of claims 2 and 4-24 under 35 U.S.C. § 112, second paragraph, as indefinite.

[6] Appellants' reply brief filed August 12, 1996 (Paper No. 55) was denied entry by the examiner in a communication mailed September 30, 1996 (Paper No. 56). Appellants' subsequent petition to enter the reply brief filed December 2, 1996 (Paper No. 59) was denied by the Office of the Director, Group 1800 in a decision on petition mailed October 14, 1997 (Paper No. 61). Therefore, appellants' reply brief was not considered in rendering our decision.

BACKGROUND

According to appellants,

> [i]n the presently claimed invention, bacterial RNA is hybridized with a primer which is complementary to a genus specific region of RNA of a particular bacteria. The 3' end of this primer is not complementary to the RNA of bacteria from another genus. If bacteria of the genus to be detected are present in the sample, the hybridized primer is elongated in the presence of a suitable polymerase and deoxyribonucleotides. Any elongation product which is formed is then hybridized with a labeled oligonucleotide which is specific for a particular species within the detected genus. The hybridization product is then detected by means of the labeled oligonucleotide. [Brief, p. 5.]

OPINION

As set forth in In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991),

> [w]here claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carry out, those of ordinary skill would have a reasonable expectation of success. See In re Dow Chemical Co., 837 F.2d 469, 473, 4 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. Id.

Mullis, Hogan and Frohman are applied as prior art against the claimed invention.

Mullis describes a process for amplifying a target nucleic acid sequence in a nucleic acid sample and then detecting the amplified target sequence (c. 2, ll. 46-50; c. 7, ll. 17-24), wherein the sample acid can be single or double stranded DNA or RNA, a DNA-RNA hybrid or mixtures thereof (c. 7, ll. 39-47), including DNA or RNA from any source, including bacteria (c. 7, l. 66 - c. 8, l. 2). For example, a single stranded nucleic acid sample containing a target sequence to be amplified (1) is hybridized with a primer complementary to the target sequence and (2) contacted with a polymerization agent, e.g., a polymerase, and the four deoxyribonucleotides to synthesize a primer extension (i.e., elongation) product, (3) the complementary strands of nucleic acid are separated and (4) the steps of strand separation and extension product synthesis are repeated until the desired quantity of the target nucleic acid sequence is produced (c. 6, ll. 56-58; c. 9, l. 5 - c. 10, l. 44). To ascertain whether a test sample contains the target sequence or not, the test sample is treated with primer, polymerase and deoxyribonucleotides as above, resulting in amplification of the target sequence if present, (5) a labeled probe capable of hybridizing to the target sequence is added and (6) if hybridization of labeled probe is detected, then the test sample contained the target sequence (c. 2, l. 63 - c. 3, l. 29). According to Mullis,

> [t]he present process is expected to be useful in detecting, in a patient DNA sample, a specific sequence associated with an infectious disease such as, e.g., Chlamydia using a biotinylated hybridization probe spanning the desired amplified sequence ... (c. 31, ll. 33-37).

Hogan describes preparing genus and species-specific hybridization probes for detection and/or quantitation of bacteria by comparing one or more sequenced rRNA variable regions from a target bacteria to one or more rRNA variable region sequences from closely related bacteria to select a sequence unique to the rRNA of the target bacteria (p. 9, l. 29 - p. 10, l. 2; p. 30, ll. 4-15).

Frohman describes production of full-length cDNA clones of low abundance mRNAs by using the DNA polymerase chain reaction to obtain copies of the region between a single point in the transcript and the 3' or 5' end.

According to the examiner,

> it would have been obvious ... to have used primers which amplified just such variable regions as identified by Hogan ..., and to have performed subsequent hybridization reactions as taught by Mullis ..., where specific probes are used. Just such probes are suggested by Mullis ..., and taught explicitly by Hogan ..., and Frohman ... . While the prior art does not explicitly state that the primers used were lacked 3' complementarity to non-target nucleic acid sequences, ... such a limitation does not render the claimed invention non-obvious but rather, is considered an obvious design component to primer design (answer, para. bridging pp. 9-10).

We have no doubt that the prior art could be modified in the manner proposed by the examiner, however the fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, we agree with appellants that the examiner has not established a prima facie case of

obviousness because the prior art does not disclose or suggest "the use of a genus-specific elongation reaction followed by a species-specific hybridization reaction" (brief, p. 10, ll. 4-5). In our judgment, the only reason or suggestion to combine the references in the manner proposed by the examiner comes from appellants' specification. Thus, we find the examiner has not carried his burden of establishing a prima facie case of obviousness and has relied on impermissible hindsight in making his determination of obviousness. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.).

Accordingly, the rejection of claims 2 and 4-24 under 35 U.S.C. § 103 as being unpatentable over Mullis in view of Hogan and Frohman is reversed.

OTHER MATTERS

Appellants indicated in the brief (pp. 2-3) that it was their belief that all the amendments made after the final rejection (Paper No. 37, mailed July 21, 1995) had been entered upon the filing of the brief. However, the examiner stated that the proposed amendment to claims 4, 15 and 24 filed October 23, 1995 (Paper No. 39) would not be entered in the advisory action mailed November 9, 1995 (Paper No. 40). The examiner

confirmed the nonentry of the proposed amendments to claims 4, 15 and 24 in the answer (Paper No. 52, pp. 2-3, § 8). By failing to respond to § 8 in the answer, appellants have acquiesced that claims 4, 15 and 24 are as stated in the answer.

CONCLUSION

To summarize, the decision of the examiner to reject claims 2 and 4-24 under 35 U.S.C. § 103 as being unpatentable over Mullis in view of Hogan and Frohman is reversed.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	)	
WILLIAM F. SMITH Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
CAROL A. SPIEGEL Administrative Patent Judge	)	

CAS/cam

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APPEAL NO. 1997-0160 - JUDGE SPIEGEL
APPLICATION NO. 08/073,985

APJ SPIEGEL

APJ WINTERS

APJ WILLIAM F. SMITH

DECISION: **REVERSED**

Prepared By: Cheryl

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FINAL TYPED: 19 Aug 00