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variable of all the genes. Such reasonably implies that the LTR is more conserved. Accordingly, one of ordinary skill in the art would have been motivated to choose that part of the HIV genome that is not subject to such high variability in the selection of primers from highly conserved regions. *See In re Preda*, 401 F.2d at 826 (noting that “in considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom”).

51. Montagnier et al., column 19, third paragraph, teaches that primers “can be prepared by well known techniques.”

52. Montagnier et al., has not been found to disclose SEQ ID NO: 1 or SEQ ID NO: 5, however, applicant, in the specification, teach how these sequences are highly conserved in HIV. Given the explicit guidance by Montagnier et al., to select just such highly conserved sequences, the selection of sequences corresponding to SEQ ID NO: 1 and SEQ ID NO: 5 would have been obvious. Further, the selection of the appropriate length would have been obvious as Montagnier et al., teaches explicitly that primers can be prepared using techniques well known in the art.

53. Applicant presents argument that Montagnier et al., teaches combining primers in a method of detecting whereas the claimed primers are to be used alone. This argument is not persuasive towards the withdrawal of the rejection as the claimed invention, for as noted above, the claims are not drawn to any method, but rather, to a composition of primers. Further, the claims do not prohibit the combining of the resultant primer pairs with other primer pairs in a multiplex amplification reaction.

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54. Independent claims 36, 41, 46, 48 and 61 require the primers to comprise a promoter region, which in dependent claims 38, 42, and 48 is limited to "a T7 promoter, a T3 promoter, or an SP6 promoter."

55. Applicant, at page 4 of the disclosure, admits:

Another technique for the amplification of nucleic acid is the so-called transcription based amplification system (TAS). The TAS method is described in International Patent Appl. no. WO 88/10315. Transcription based amplification techniques usually comprise treating target nucleic acid with two oligonucleotides one of which comprises a promoter sequence, to generate a template including a functional promoter. Multiple copies of RNA are transcribed from said template and can serve as a basis for further amplification.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295. EP 408295 is primarily concerned with a two-enzyme transcription based amplification method. Transcription based amplification methods, such as the NASBA method as described in EP 329822, are usually employed with a set of oligonucleotides, one of which is provided with a promoter sequence that is recognized by a DNA dependent RNA polymerase such as, for example, T7 polymerase. Several modifications of transcription based techniques are known in the art.

In contrast to RT-PCR, NASBA, which is based on RNA transcription by T7 RNA polymerase (Kievits et al., 1991; Compton, 1991), does not need differentiation between RNA- and DNA- derived amplification products since it uses RNA as its principal target. NASBA enables specific amplification of RNA targets even in a background of DNA.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295... One or more "promoter-primers" (oligonucleotides provided with a promoter sequence) may be used in transcription based amplification techniques, optionally combined with the use of one or more oligonucleotides that are not provided with a promoter sequence. For RNA amplification, a transcription based amplification technique, is a preferred technology.

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In each of the above-reproduced paragraphs, applicant has provided a summary of the disclosures of the various documents. Such statements, while not labeled as “prior art,” are considered to be admissions of prior art.

56. In view of the admitted state of the art where primers comprising a promoter region, such as T7, are used in transcription based amplification methods, and that the inclusion of the T7 promoter in such primers was known in the art, and that NASBA does not need differentiation between RNA- and DNA-derived amplification products, one of ordinary skill in the art at the time of the invention would have been motivated to have included just such a promoter on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences, be they RNA as found in the viral particles, or DNA, as is found when HIV-1 has integrated into a hosts genome (proviral sequence).

57. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007):

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

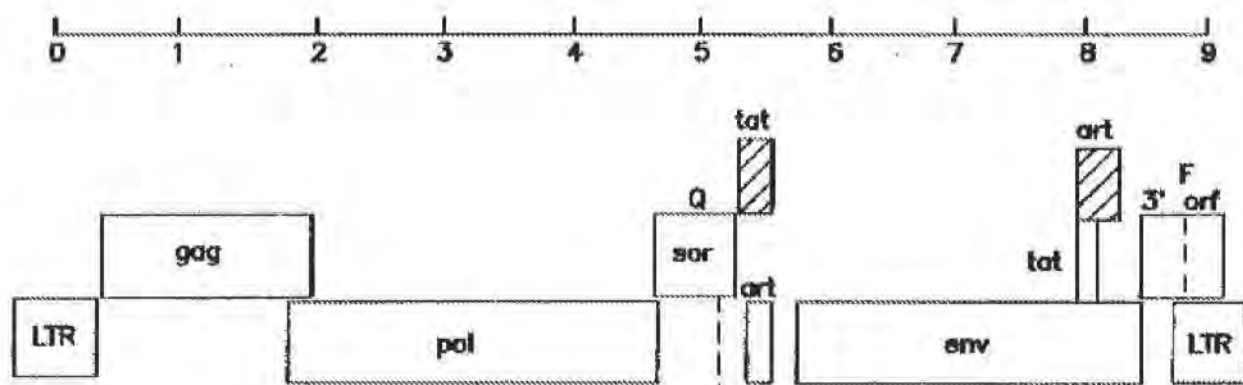
58. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes “background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR* at 1396.

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59. Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

60. The prior art of record explicitly directs one to “highly conserved” regions of the HIV genome, and specifically identifies the LTR of HIV. Clearly, there exists but a finite number of “highly conserved” regions within the LTR of HIV.

61. Montagnier et al., in FIG. 1, shows that the LTR region is less than 1 kb in size.



62. Given such a small target area, and specific guidance as to where and what to be looking for, there exists but a finite number of identified, predictable solutions. In light of the extreme interest in one being able to identify the various types of HIV, and the specific guidance provided, said ordinary artisan would have been both amply motivated and would have had a most reasonable expectation of success.

63. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

64.

Response to argument

65. Agreement is reached with applicant at page 9 of the response of 09 May 2012, hereinafter the response, in that the cancelation of claim 4 and 34 has rendered moot the rejection of same.

66. At page 11, bridging to page 12 of the response, argument is presented that statements made by applicant are not admissions of prior art and that the specification does not "identify anything as prior art." Further at page 12 of the response, applicant states:

Applicants point out that the specification does not contain a defined background section per se as there are no section titles in the specification. Moreover, even if the portion of the specification containing the cited disclosure is considered to be the background section, the BPAI makes it clear that there is no automatic conclusion that a statement therein is prior art. The Examiner has not set forth any underlying facts and reasoning leading to the conclusion that the statement constitutes a prior art admission as required by the BPAI. Thus, the Examiner's use of the statement as an admission of prior art by Applicants is improper.

67. The above argument has been considered and has not been found persuasive. As noted above, the case at hand is analogous to that of *Ex parte Shirley* in that there is no part of the disclosure directed to "prior art," or that the specification identifies any of the cited publications as "prior art." Contrary to applicant's underlying facts and reasoning have been provided. Accordingly, and like *Ex parte Shirley*, the absence of applicant employing such a label does not shield applicant from these prior-art statements from being used as such.

68. At pages 13 and 18 of the response argument is presented in that impermissible hindsight reasoning was used to provide motivation for one of skill in the art to produce the claimed primers. This argument has not been found persuasive as the rejection clearly sets out specific publications which applicant admits disclose methods not only for selecting primers for HIV, but

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also the need for being able to detect the many variants of HIV. Additionally, the rejection clearly set out that it was known in the art years prior to the effective filing date that the *env* gene of HIV-1 was not only highly variable, but the most variable region of the HIV-1 genome.

69. Applicant, at pages 13-16, 18, and 19, asserts that the rejection cannot be maintained for *Montagnier et al.*, in effect teach away from the LTR region by also suggesting highly conserved sequences in other parts of the HIV-1 genome. This argument has been considered and has not been found persuasive. As noted above, it was known in the art that the *env* gene was the most variable. It stands to reason that if the *env* was the most variable, then the LTR is one of, if not the most highly conserved region. *See In re Preda*, 401 F.2d at 826 (noting that “in considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom”). With *Montagnier et al.*, teaching one of ordinary skill in the art to produce primers that are directed to highly conserved nucleotide sequences, and then specifically identifies the LTR region, and said artisan being well aware that the *env* gene is not only highly variable but the most variable region in the HIV genome, said ordinary artisan would have been amply motivated to have selected primers that are derived from those highly conserved regions of the HIV-1 LTR. Such a showing does clearly speak to the existence of a finite number of identified, predictable solutions to the art-recognized problem.

70. Applicant, at page 18 of the response states:

The Examiner states that the aspect of the 3' terminal nucleotide sequences not being defined is significant and calls into question the ability of the primers to function, much less render a superior result in an undefined and non-claimed assay, citing to Sommer and Tautz (*Nucleic Acids Res.* 17:6749 (1989)). (Office Action, pages 12-13).

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Applicants respectfully disagree. The present claims require the primer set to be functional to amplify the target sequence. Primer sets that are incapable of amplifying the target are not encompassed within the scope of the claims. Thus, the Examiner's concern that the claims encompass nonfunctional primers is not valid. One of ordinary skill in the art of hybridization and amplification assays would be well aware of the physical requirements for a functional primer. In fact, Sommer and Tautz cited by the Examiner provides a good example of the knowledge in the art regarding homology requirements for primers.

71. The above argument has been considered and has not been found persuasive. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

72. In the present case, the claims recite the functional limitation: "wherein said primers amplify the target sequence located within the LTR region of the HIV-I genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur" (emphasis added). For purposes of examination, the clause "under conditions whereby nucleic acid amplification can occur" has been construed as encompassing any conditions, including those where less than "superior results" (response at page 18, third paragraph) are obtained. As applicant noted, the publication of Sommer and Tautz does teach just how little complementarity (just 2 nucleotides at the 3' terminus of a primer) is needed in order to satisfy "conditions whereby nucleic acid amplification can occur."

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73. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

Conclusion

74. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

75. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

76. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

77. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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78. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

Notice of References Cited	Application/Control No. 11/108,233		Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson		Art Unit 1634	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,122,457	06-1992	Reim et al.	435/69.1
*	B	US-4,772,547	09-1988	Heimer et al.	435/5
*	C	US-4,963,532	10-1990	Carter, William A.	514/44R
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)			
*	U	Sommer and Tautz, "Minimal homology requirements for PCR primers," Nucleic Acids Research, vol. 17, No. 16, 1989, page 6749.			
	V				
	W				
	X				

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.



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BIB DATA SHEET

CONFIRMATION NO. 5814

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
11/108,233	04/18/2005	435	1634	9310-22CT		
RULE						
APPLICANTS Jaap Goudsmit, Amsterdam, NETHERLANDS; Pieter Oudshoorn, Michielsgestel, NETHERLANDS; Suzanne Jurriaans, Monnickendam, NETHERLANDS; Vladimir Vladimirovich Lukashov, Dienen, NETHERLANDS;						
** CONTINUING DATA ***** This application is a CON of 09/463,352 01/21/2000 PAT 6,881,537 which is a 371 of PCT/EP98/04945 08/05/1998						
** FOREIGN APPLICATIONS ***** EUROPEAN PATENT OFFICE (EPO) 97202455.8 08/08/1997						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/18/2005						
Foreign Priority claimed	☒ Yes ☐ No	☐ Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
35 USC 119(a-d) conditions met	☒ Yes ☐ No	Initials	NETHERLANDS	1	25	6
Verified and Acknowledged	/BRADLEY L SISSON/ Examiner's Signature					
ADDRESS						
MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627 UNITED STATES						
TITLE						
NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1						
FILING FEE RECEIVED	FEES: Authority has been given in Paper			☐ All Fees		
2500	No. _____ to charge/credit DEPOSIT ACCOUNT			☐ 1.16 Fees (Filing)		
	No. _____ for following:			☐ 1.17 Fees (Processing Ext. of time)		
				☐ 1.18 Fees (Issue)		
				☐ Other _____		
				☐ Credit		



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814
20792 7590 07/23/2012 MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			EXAMINER SISSON, BRADLEY L	
			ART UNIT 1634	PAPER NUMBER
			MAIL DATE 07/23/2012	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

11/108,233

Applicant(s)

GOUDSMIT ET AL.

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 May 2012.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 36,38,41,42,46,48,50,52,53,55,56 and 58-61 is/are pending in the application.
- 5a) Of the above claim(s) 50,52,53,55 and 56 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 36,38,41,42,46,48 and 58-61 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 07 October 2011 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/463,352.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

Withdrawal of Finality

1. The finality of the prior Office action is hereby withdrawn. The period for applicant filing a response is reset with the mailing of the instant Office action.

Election/Restrictions

2. Claims 50, 52, 53, 55, and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on -5 November 2007.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/463,352, filed on 21 January 2000.

Drawings

4. The drawings were received on 07 October 2011. These drawings are acceptable.

Terminal Disclaimer

5. The terminal disclaimer filed on 26 May 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent

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Application 11/372,577 has been reviewed and is accepted. The terminal disclaimer has been recorded.

6. The terminal disclaimer filed on 01 May 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent 6,881,537 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Attention is directed to *Mayo Collaborative Services v. Prometheus Laboratories, Inc. (Mayo)* 101 USPQ2d 1961, 1965-1966 (SC 2012). As stated therein:

“Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.” *Gottschalk v. Benson*, 409 U. S. 63, 67 (1972). And monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it. (Emphasis added)

9. Claims 36, 41, 46, and 61 are each independent. Claim 36 is deemed representative and, for convenience, is reproduced below.

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36. (Currently Amended) A pair of oligonucleotide primers for the amplification of a target sequence located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer comprises

(1) a first oligonucleotide being 10-~~25~~ 30 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AOA GA; and

(2) a promoter operably linked to said first oligonucleotide; and

wherein said second primer comprises a second oligonucleotide being 10-~~26~~ 30 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers first and second oligonucleotides amplify the target sequence located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

10. In the present case, the claims are drawn to compositions comprising nucleic acids that can serve as primers in the amplification of Long Terminal Repeat (LTR) sequences of any variant of HIV-1. As presently worded, there must be two primers, with one (applicant's "first hybridizing oligonucleotide") comprising at least 10 nucleotides of SEQ ID NO. 1 and the other (applicant's "second hybridizing oligonucleotide") comprising at least 10 nucleotides of SEQ ID NO. 5.

11. The primers/hybridizing oligonucleotides can be 26 nucleotides in length. However, in the case of the "first hybridizing oligonucleotide," the molecule is to also "comprise" any desired "promoter," be it known or not. Dependent claims 38, 42, and 48 specify "the promoter is a T7 promoter, a T3 promoter, or an SP6 promoter." The use of the term "a" has been construed to encompass any and all variants of each of the promoters, be it known or unknown, and be it naturally occurring and/or the result of genetic manipulation. US Patent 5,122,457 (Reim et al.),

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column 6, teaches of there being a variety of T7 promoters and that they have been classified into at least three classes. At column 12, lines 49-53, Reim et al., teach that a T7 promoter/gene they isolated is 1136 nucleotides in length. Given that the “first primer” is to comprise both “a first oligonucleotide” and a “promoter operably linked to said first oligonucleotide,” the “oligonucleotide being 10-26 nucleotides in length” is actually in excess of 1140 nucleotides in length when there are but 10 nucleotides in common with SEQ ID NO. 1, and can be in excess of 1160 nucleotides when the “first oligonucleotide” is some 26 nucleotides in length.

12. Using the first primer as an example. It is noted that the claims do not specify the nucleotide sequence for those residues that are not found in SEQ ID NO. 1. Using the example of where there need be but 10 consecutive nucleotides of SEQ IDNO. 1 present, and with the primer being anywhere from 10 to 26 nucleotides in length (ignoring the presence of the promoter), and substituting each of the common four nucleotides for each of the possible positions for just one terminus, e.g., the 3' terminus, of the primer, one finds that there are some 5,726,623,060 possible different oligonucleotides to choose from. The same holds true for the 5' terminus as well as for both termini of the second primer. Ignoring the genera of promoter sequences encompassed by the claims, it becomes evident that applicant is claiming members selected from a genus of some 22.9 billion oligonucleotides. A review of the disclosure finds only 14 different sequences, of which SEQ ID NO. 1 and 5 are included.

13. In accordance with independent claims 36, 41, 46, and 61, the conditions for hybridization are limited only in that “nucleic acid amplification can occur.” Such language has been construed as encompassing any level of amplification, including less than specific amplification. While the claims do recite the limitation that they are to be useful in the

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amplification of the LTR of HIV-1, there is no requirement that they actually bind to the LTR of any HIV-1. It is noted with particularity that the genome of HIV-1 contains a LTR at both ends. It stands to reason, therefore, that any primer that anneals to any region of the genome of HIV-1, be it within the LTR or not, will ultimately result in amplification of an LTR if the primer extension reaction is allowed to go to completion- the end of the HIV-1 genome/nucleotide sequence. In support of the position that effective priming can occur where only two or three nucleotides at the 3' terminus of the primer binds, attention is directed to the publication of Sommer and Tautz, "Minimal homology requirements for PCR primers," *Nucleic Acids Research*, vol. 17, No. 16, 1989, page 6749. As stated therein:

Primers with a length between 17-20nt need at least three homologous nucleotides at their 3'-end for successful priming. Weak priming was however also obtained with a long primer having only 2 nucleotides homology (Table 1.n). Surprisingly, the remainder of the primer needs only very little homology with the target sequence.

14. As noted above, the claims fairly encompass embodiments where some 16 consecutive nucleotides do not need to be complementary to SEQ ID NO. 1 and/or 5 and do not need to be complementary to any HIV-1 LTR.

15. As presently worded, the claims fairly encompass nucleotides that will hybridize to any region of any isolate of HIV-1, be it known at the time of filing or yet to be discovered. Similarly, the requirement that the first primer also comprise a "promoter," which has been construed as encompassing not only any promoter known at the time of filing, but also those that have yet to be discovered.

16. By claiming the primer pairs in such general terms, the claims fairly encompass embodiments that are not only known, but also seek to block future development in the area of

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art. Accordingly, the claims are deemed to focus on the natural laws and do not “also contain other elements or a combination of elements... [so] to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself.”

17. For the above reasons, and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim Rejections - 35 USC § 112

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

20. Attention is directed to MPEP 904.01.

The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

21. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of

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patentability. *In re Philips Industries v. State Stove & Mfg. Co., Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

22. As set forth in *In re Alonso* 88 USPQ2d 1849 (Fed. Cir. 2008), at 1851:

The written description requirement of 35 U.S.C. § 112, ¶ 1, is straightforward: “The specification shall contain a written description of the invention” To satisfy this requirement, the specification must describe the invention in sufficient detail so “that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought.” *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997); see also *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 [76 USPQ2d 1724] (Fed. Cir. 2005); *Eiselstein v. Frank*, 52 F.3d 1035, 1039 [34 USPQ2d 1467] (Fed. Cir. 1995).

Alonso at 1852:

A genus can be described by disclosing: (1) a representative number of species in that genus; or (2) its “relevant identifying characteristics,” such as “complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” *Enzo*, 323 F.3d at 964.

23. In applying the test as set forth in *Alonso*, it is noted that applicant is claiming compositions comprising nucleic acids that can serve as primers in the amplification of Long Terminal Repeat (LTR) sequences of any variant of HIV-1. As presently worded, there must be two primers, with one (applicant’s “first hybridizing oligonucleotide”) comprising at least 10 nucleotides of SEQ ID NO. 1 and the other (applicant’s “second hybridizing oligonucleotide”) comprising at least 10 nucleotides of SEQ ID NO. 5.

24. The primers/hybridizing oligonucleotides can be 26 nucleotides in length. However, in the case of the “first hybridizing oligonucleotide,” the molecule is to also “comprise” any desired

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“promoter,” be it known or not. Dependent claims 38, 42, and 48 specify “the promoter is a T7 promoter, a T3 promoter, or an SP6 promoter.” The use of the term “a” has been construed to encompass any and all variants of each of the promoters, be it known or unknown, and be it naturally occurring and/or the result of genetic manipulation. US Patent 5,122,457 (Reim et al.), column 6, teaches of there being a variety of T7 promoters and that they have been classified into at least three classes. At column 12, lines 49-53, Reim et al., teach that a T7 promoter they isolated is 1136 nucleotides in length. Given that the “first primer” is to comprise both “a first oligonucleotide” and a “promoter operably linked to said first oligonucleotide,” the “oligonucleotide being 10-26 nucleotides in length” is actually in excess of 1140 nucleotides in length when there are but 10 nucleotides in common with SEQ ID NO. 1, and can be in excess of 1160 nucleotides when the “first oligonucleotide” is some 26 nucleotides in length.

25. Using the first primer as an example, it is noted that the claims do not specify the nucleotide sequence for those residues that are not found in SEQ ID NO. 1. Using the example of where there need be but 10 consecutive nucleotides of SEQ ID NO. 1 present, and with the primer being anywhere from 10 to 26 nucleotides in length (ignoring the presence of the promoter), and substituting each of the common four nucleotides for each of the possible positions for just one terminus, e.g., the 3' terminus, of the primer, one finds that there are some 5,726,623,060 possible different oligonucleotides to choose from. The same holds true for the 5' terminus as well as for both termini of the second primer. Ignoring the genera of promoter sequences encompassed by the claims, it becomes evident that applicant is claiming members selected from a genus of some 22.9 billion oligonucleotides. A review of the disclosure finds only 14 different sequences, of which SEQ ID NO. 1 and 5 are included.

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26. In accordance with independent claims 36, 41, 46, and 61, the conditions for hybridization are limited only in that "nucleic acid amplification can occur." Such language has been construed as encompassing any level of amplification, including less than specific amplification. While the claims do recite the limitation that they are to be useful in the amplification of the LTR of HIV-1, there is no requirement that they actually bind to the LTR of any HIV-1. It is noted with particularity that the genome of HIV-1 contains a LTR at both ends. It stands to reason, therefore, that any primer that anneals to any region of the genome of HIV-1, be it within the LTR or not, and be it to a conserved region or not, will ultimately result in amplification of the LTR if the primer extension reaction is allowed to go to completion- the end of the HIV-1 genome/nucleotide sequence, and/or the amplification of any other (non-target) nucleic acid present that also has the same recognition sequence. In support of the position that effective priming can occur where only two or three nucleotides at the 3' terminus of the primer binds, attention is directed to the publication of Sommer and Tautz, "Minimal homology requirements for PCR primers," *Nucleic Acids Research*, vol. 17, No. 16, 1989, page 6749. As stated therein:

Primers with a length between 17-20nt need at least three homologous nucleotides at their 3'-end for successful priming. Weak priming was however also obtained with a long primer having only 2 nucleotides homology (Table 1.n). Surprisingly, the remainder of the primer needs only very little homology with the target sequence.

27. As noted above, the claims fairly encompass embodiments where some 16 consecutive nucleotides do not need to be complementary to SEQ ID NO. 1 and/or 5 and do not need to be complementary to any HIV-1 LTR.

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28. As presently worded, the claims fairly encompass nucleotides that will hybridize to any region of any isolate of HIV-1, be it known at the time of filing or yet to be discovered.

Similarly, the requirement that the first primer also comprise a "promoter," which has been construed as encompassing not only any promoter known at the time of filing, but also those that have yet to be discovered. The disclosure of 2 sequences has not been found to satisfy either prong of the written description test of *Alonso*.

29. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Response to argument

30. Applicant, at page 18 of the response of 09 May 2012 states:

Applicants have identified hybridization sites in the HIV-1 genome that provide superior results for detection of HIV-1 variants. Given the disclosure of these preferred sites by Applicants and a sequence of at least 10 or at least 15 nucleotides of these preferred sites and a maximum length of 26 nucleotides, one of ordinary skill in the art could readily produce functional primers. Furthermore, one of ordinary skill in the art would reasonably expect that any of these functional primers comprising at least 10 or at least 15 nucleotides of these preferred sites would provide the same superior results as the primers exemplified in the present specification because each of the primers are expected to hybridize to the same preferred sites. The Examiner has not provided any evidence to show why there would not be such a reasonable expectation and therefore why the showing of superior results is not commensurate with the scope of the claims.

31. Applicant, at page 17 of the response of 09 May 2012, hereinafter the response, states:

Independent claims 36, 41, and 46 are directed in part to oligonucleotide primers that are 10-26 nucleotides in length and comprise at least 10 nucleotides of SEQ ID NO:1 or SEQ ID NO:5. Thus, the claimed primers have as few as zero nucleotides "undefined" and a maximum of 16 nucleotides "undefined." Dependent claims 58-60 are directed in part to oligonucleotide primers that are 15-26 nucleotides in length and comprise at least 15 nucleotides of SEQ ID NO:1 or SEQ ID NO:5. Thus, the claimed primers have as few as zero nucleotides "undefined" and a maximum of 11 nucleotides "undefined."

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Furthermore, the nucleotides are not in fact "undefined" as suggested by the Examiner. The claims require that the primers function to amplify the target sequence located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur. Thus, the allegedly "undefined" nucleotides are limited structurally to those that will ensure adequate hybridization of the primers to the target sequence in a manner such that primer extension

32. The above arguments have been considered and have not been found persuasive towards the withdrawal of the rejection. As set forth above, the claims fairly encompass oligonucleotides that hybridize under any conditions to the target, and that the useful primers are to be selected from a genus that numbers in the 10s of billions. The claims do not require that the portion of the primer that is actually responsible for priming be conserved at all. Rather, the claims fairly encompass primers that will hybridize to any nucleotide sequence that, while is found somewhere in HIV-1, can also be found in any other source of DNA, e.g., an recognition sequence for a restriction endonuclease (e.g., *EcoRI*) that is found in human DNA as well as in the HIV-1 genome. As noted above, any primer that hybridizes at any point of an HIV-1 genome can be considered one that will result in the amplification of HIV-1 LTR sequences, as there is an LTR on each end of the HIV-1 genome. Given such lack of specificity, one would have no expectation that any "superior results," or even useful results, would be obtained as one would not be able to distinguish between an amplicon from human DNA and a like amplicon generated from HIV-1 genome.

33. Agreement is reached with applicant where, at page 18 of the response, is stated: "Primer sets that are incapable of amplifying the target are not encompassed within the scope of the claims." However, as noted above, the claims do not exclude any primer that is also capable of binding to non-conserved nucleotide sequences, e.g., nucleotide sequences that are found in any

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of a number of diverse sources, such as restriction endonuclease recognition sequences.

Applicant has not provided an adequate description of those primers that are useful from those that are not so to reasonably suggest that applicant had possession of the full genus of useful primes when, as shown above, one is forced to select from tens of billions of candidate primes.

34. Applicant's argument that the skilled artisan would be able to develop useful probes speaks to applicant not having possession of the genus of probes claimed. It is noted with particularity that the claims are not drawn to a method of making probes, but rather, to the probes themselves. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966;

Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

35. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claim Rejections - 35 USC § 103

36. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

37. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459

(1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

38. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

39. Claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

40. Claims 36, 41, 46, and 61 are independent. Claim 36 is deemed representative and, for convenience, is reproduced below.

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36. (Currently Amended) A pair of oligonucleotide primers for the amplification of a target sequence located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer comprises

(1) a first oligonucleotide being 10-26 50 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably linked to said first oligonucleotide; and

wherein said second primer comprises a second oligonucleotide being 10-26 50 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers first and second oligonucleotides amplify the target sequence located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

41. Attention is directed to MPEP 904.01.

The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

42. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

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43. The claims under consideration are drawn to a composition- primers useful in the amplification of a target nucleotide sequence found within the Long Terminal Repeat (LTR) region of Human Immunodeficiency Virus (HIV-1). It is further noted that the claims under consideration are not drawn to a method. Additionally, it is noted that the claims do not prohibit one from combining the claimed primer pairs with other probes/primers in a method of use.

44. Attention is directed to MPEP 2129 [R-6], Admissions as Prior Art, which states in part:

I. ADMISSIONS BY APPLICANT CONSTITUTE PRIOR ART

A statement by an applicant >in the specification or made< during prosecution identifying the work of another as “prior art” is an admission **>which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988).

45. Attention is also directed to *Ex parte Shirley*, (BPAI, 2009) Appeal No. 2009002352, which, at pages 21 and 26, states:

The Specification’s omission of the term “prior art” and inclusion of the prior-art disclaimer may initially appear to indicate that Appellants do not consider the single-step soft bake process to constitute prior art. To place these latter, contraindicative factors into the proper context though, we note that patent-application drafters regularly endeavor to avoid the indiscriminate or imprudent use of the descriptive label, “prior art.” See *Riverwood Intern. Corp. v. R.A. Jones & Co., Inc.*, 324 F.3d 1346, 1354 (Fed. Cir. 2003) (citing *In re Fout*, 675 F.2d 297, 300 (CCPA 1982)) for the proposition that “section 102 is not the only source of ... prior art. Valid prior art may be created by the admissions of the parties”; *In re Nomiya*, 509 F.2d 566, 571 (CCPA 1975) (holding that an Applicant’s labeling of certain figures as “prior art,” *ipsissimis verbis*, constituted an admission that the pictured subject matter was prior art relative to Applicant’s invention); MPEP § 21294 (instructing that “the examiner must determine whether the subject matter identified as ‘prior art’ is applicant’s own work, or the work of another. In the absence of another credible explanation, examiners should treat such subject matter as the work of another”).

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The Specification's omission of the term "prior art" and inclusion of the boilerplate prior-art disclaimer do not change our conclusion. In view of the record as a whole, these factors are ineffective in shielding Appellants from having their prior-art admissions treated as such.

46. Upon review of the instant disclosure it is noted that there is no part of the disclosure that is labeled as being directed to "Prior Art," or that any of the cited documents constitute "prior art." However, the instant disclosure has been found to specifically identify documents that were published prior to the effective filing date of the subject application. Such documents and applicant's characterization as to what they disclose are considered to be admissions as to prior art. Additionally, a review of the disclosure has also found statements by applicant as to what was known in the art at the time of the invention. Such statements are also considered to be admissions of prior art.

47. Applicant, at page 2 of the disclosure admits:

Some regions are more prone to sequence variation than others. Especially in the *env* domain sequence variation can be as high as 30% between members of the different subtypes. Ideally, primer selection should be based on knowledge of interstrain variability in candidate primer sequences and the consequences of mismatching at primer sites. McCutchan et al, J.AIDS, 4, 1241-1250, 1991, used PCR to make a genetic comparison of different HIV-1 isolates. Using anchored PCR (varying sense primers were used with a constant antisense primer, primers were chosen from relatively conserved regions in gag, env and LTR)

48. Upon review of the above statement, it is not clear if the characterization of the percent variability of the *env* gene is an admission of prior art or whether it is information obtained by applicant. In answering this question, it is noted that US Patent 4,772,547 (Heimer et al.), which was published nearly 9 years prior to the effective filing date of the subject application, teaches in column 5, third paragraph, that the variability of the *env* gen can be as much as 20 %.

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Additionally, US Patent 4,963,532 (Carter), which issued 16 October 1990, nearly 7 years prior to the effective filing date of the subject application, states in column 1, lines 32-34: "The most variable region of the HIV genome is the envelope (*env*) gene..." In view of the state of the art at the time of filing, these statements are deemed to be admissions of prior art.

49. Applicant, at page 2, last paragraph, bridging to page 3, of the disclosure states:

Research aimed at identifying suitable primer sets for the reliable amplification of HIV-1 derived nucleic acid sequences has been ongoing for the past years. Engelbrecht et al., *J. Virol. Meth.*, 55, 391-400, 1995, describe a study aimed at the development of a specific and sensitive PCR protocol using *env*, *gag* and LTR primer pairs to detect subtypes present in the Western Cape, South Africa. Twenty four strains of which it was known that they belonged to subtypes B, C and D were analyzed.

50. Applicant, at page 3, last paragraph, admits:

Various techniques for amplifying nucleic acid are known in the art.

51. Montagnier et al., column 19, bridging to column 20, teach explicitly of preparing primers specific for HIV and that these primers are to be "derived from highly conserved regions of the viral genome, such as the LTR..." Given the state of the art and the explicit guidance to identify primers in this very region, one would have been amply motivated and would have also had a most reasonable expectation of success.

52. Applicant, in the response of 09 May 2012, presents argument that Montagnier et al., also suggests using other regions of the HIV genome in the production of primers and that as such, one would not be directed to the LTR region. This argument has been considered and has not been found persuasive. As noted above, the *env* gene was known in the art to be the most variable of all the genes. Such reasonably implies that the LTR is more conserved. Accordingly,

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one of ordinary skill in the art would have been motivated to chosen that part of the HIV genome that is not subject to such high variability in the selection of primers from highly conserved regions. *See In re Preda*, 401 F.2d at 826 (noting that “in considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom”).

53. Montagnier et al., column 19, third paragraph, teaches that primers "can be prepared by well known techniques."

54. Montagnier et al., has not been found to disclose SEQ ID NO: 1 or SEQ ID NO: 5, however, applicant, in the specification, teach how these sequences are highly conserved in HIV. Given the explicit guidance by Montagnier et al., to select just such highly conserved sequences, the selection of sequences corresponding to SEQ ID NO: 1 and SEQ ID NO: 5 would have been obvious. Further, the selection of the appropriate length would have been obvious as Montagnier et al., teaches explicitly that primers can be prepared using techniques well known in the art.

55. Applicant presents argument that Montagnier et al., teaches combining primers in a method of detecting whereas the claimed primers are to be used alone. This argument is not persuasive towards the withdrawal of the rejection as the claimed invention, for as noted above, the claims are not drawn to any method, but rather, to a composition of primers. Further, the claims do not prohibit the combining of the resultant primer pairs with other primer pairs in a multiplex amplification reaction.

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56. Independent claims 36, 41, 46, 48 and 61 require the primers to comprise a promoter region, which in dependent claims 38, 42, and 48 is limited to "a T7 promoter, a T3 promoter, or an SP6 promoter."

57. Applicant, at page 4 of the disclosure, admits:

Another technique for the amplification of nucleic acid is the so-called transcription based amplification system (TAS). The TAS method is described in International Patent Appl. no. WO 88/10315. Transcription based amplification techniques usually comprise treating target nucleic acid with two oligonucleotides one of which comprises a promoter sequence, to generate a template including a functional promoter. Multiple copies of RNA are transcribed from said template and can serve as a basis for further amplification.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295. EP 408295 is primarily concerned with a two-enzyme transcription based amplification method. Transcription based amplification methods, such as the NASBA method as described in EP 329822, are usually employed with a set of oligonucleotides, one of which is provided with a promoter sequence that is recognized by a DNA dependent RNA polymerase such as, for example, T7 polymerase. Several modifications of transcription based techniques are known in the art.

In contrast to RT-PCR, NASBA, which is based on RNA transcription by T7 RNA polymerase (Kievits et al., 1991; Compton, 1991), does not need differentiation between RNA- and DNA- derived amplification products since it uses RNA as its principal target. NASBA enables specific amplification of RNA targets even in a background of DNA.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295... One or more "promoter-primers" (oligonucleotides provided with a promoter sequence) may be used in transcription based amplification techniques, optionally combined with the use of one or more oligonucleotides that are not provided with a promoter sequence. For RNA amplification, a transcription based amplification technique, is a preferred technology.

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In each of the above-reproduced paragraphs, applicant has provided a summary of the disclosures of the various documents. Such statements, while not labeled as “prior art,” are considered to be admissions of prior art.

58. In view of the admitted state of the art where primers comprising a promoter region, such as T7, are used in transcription based amplification methods, and that the inclusion of the T7 promoter in such primers was known in the art, and that NASBA does not need differentiation between RNA- and DNA-derived amplification products, one of ordinary skill in the art at the time of the invention would have been motivated to have included just such a promoter on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences, be they RNA as found in the viral particles, or DNA, as is found when HIV-1 has integrated into a hosts genome (proviral sequence).

59. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007):

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

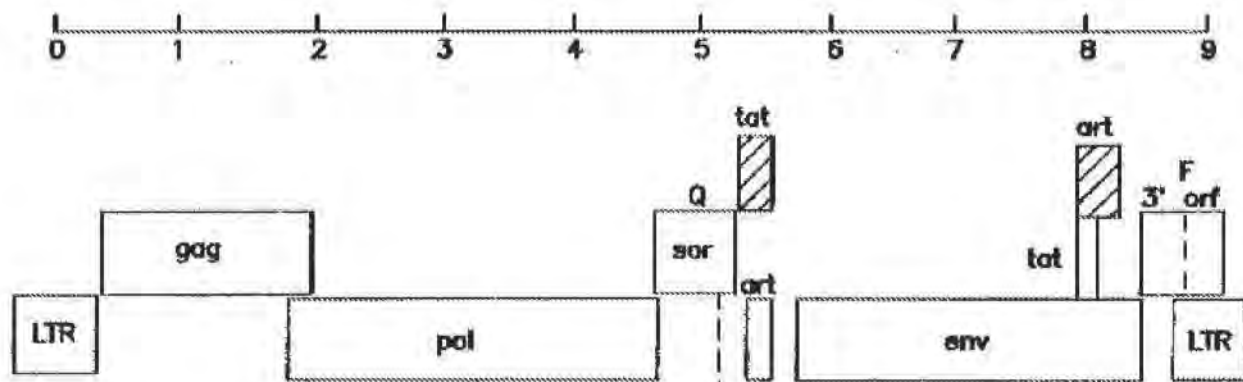
60. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes “background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR* at 1396.

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61. Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

62. The prior art of record explicitly directs one to “highly conserved” regions of the HIV genome, and specifically identifies the LTR of HIV. Clearly, there exists but a finite number of “highly conserved” regions within the LTR of HIV.

63. Montagnier et al., in FIG. 1, shows that the LTR region is less than 1 kb in size.



64. Given such a small target area, and specific guidance as to where and what to be looking for, there exists but a finite number of identified, predictable solutions. In light of the extreme interest in one being able to identify the various types of HIV, and the specific guidance provided, said ordinary artisan would have been both amply motivated and would have had a most reasonable expectation of success.

65. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

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Response to argument

66. Agreement is reached with applicant at page 9 of the response of 09 May 2012, hereinafter the response, in that the cancelation of claim 4 and 34 has rendered moot the rejection of same.

67. At page 11, bridging to page 12 of the response, argument is presented that statements made by applicant are not admissions of prior art and that the specification does not "identify anything as prior art." Further at page 12 of the response, applicant states:

Applicants point out that the specification does not contain a defined background section per se as there are no section titles in the specification. Moreover, even if the portion of the specification containing the cited disclosure is considered to be the background section, the BPAI makes it clear that there is no automatic conclusion that a statement therein is prior art. The Examiner has not set forth any underlying facts and reasoning leading to the conclusion that the statement constitutes a prior art admission as required by the BPAI. Thus, the Examiner's use of the statement as an admission of prior art by Applicants is improper.

68. The above argument has been considered and has not been found persuasive. As noted above, the case at hand is analogous to that of *Ex parte Shirley* in that there is no part of the disclosure directed to "prior art," or that the specification identifies any of the cited publications as "prior art." Contrary to applicant's underlying facts and reasoning have been provided. Accordingly, and like *Ex parte Shirley*, the absence of applicant employing such a label does not shield applicant from these prior-art statements from being used as such.

69. At pages 13 and 18 of the response argument is presented in that impermissible hindsight reasoning was used to provide motivation for one of skill in the art to produce the claimed primers. This argument has not been found persuasive as the rejection clearly sets out specific publications which applicant admits disclose methods not only for selecting primers for HIV, but

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also the need for being able to detect the many variants of HIV. Additionally, the rejection clearly set out that it was known in the art years prior to the effective filing date that the *env* gene of HIV-1 was not only highly variable, but the most variable region of the HIV-1 genome.

70. Applicant, at pages 13-16, 18, and 19, asserts that the rejection cannot be maintained for Montagnier et al., in effect teach away from the LTR region by also suggesting highly conserved sequences in other parts of the HIV-1 genome. This argument has been considered and has not been found persuasive. As noted above, it was known in the art that the *env* gene was the most variable. It stands to reason that if the *env* was the most variable, then the LTR is one of, if not the most highly conserved region. See *In re Preda*, 401 F.2d at 826 (noting that “in considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom”). With Montagnier et al., teaching one of ordinary skill in the art to produce primers that are directed to highly conserved nucleotide sequences, and then specifically identifies the LTR region, and said artisan being well aware that the *env* gene is not only highly variable but the most variable region in the HIV genome, said ordinary artisan would have been amply motivated to have selected primers that are derived from those highly conserved regions of the HIV-1 LTR. Such a showing does clearly speak to the existence of a finite number of identified, predictable solutions to the art-recognized problem.

71. Applicant, at page 18 of the response states:

The Examiner states that the aspect of the 3' terminal nucleotide sequences not being defined is significant and calls into question the ability of the primers to function, much less render a superior result in an undefined and non-claimed assay, citing to Sommer and Tautz (*Nucleic Acids Res.* 17:6749 (1989)). (Office Action, pages 12-13).

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Applicants respectfully disagree. The present claims require the primer set to be functional to amplify the target sequence. Primer sets that are incapable of amplifying the target are not encompassed within the scope of the claims. Thus, the Examiner's concern that the claims encompass nonfunctional primers is not valid. One of ordinary skill in the art of hybridization and amplification assays would be well aware of the physical requirements for a functional primer. In fact, Sommer and Tautz cited by the Examiner provides a good example of the knowledge in the art regarding homology requirements for primers.

72. The above argument has been considered and has not been found persuasive. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

73. In the present case, the claims recite the functional limitation: "wherein said primers amplify the target sequence located within the LTR region of the HIV-I genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur" (emphasis added). For purposes of examination, the clause "under conditions whereby nucleic acid amplification can occur" has been construed as encompassing any conditions, including those where less than "superior results" (response at page 18, third paragraph) are obtained. As applicant noted, the publication of Sommer and Tautz does teach just how little complementarity (just 2 nucleotides at the 3' terminus of a primer) is needed in order to satisfy "conditions whereby nucleic acid amplification can occur."

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74. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

Conclusion

75. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

76. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

77. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

Notice of References Cited	Application/Control No. 11/108,233		Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson		Art Unit 1634	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,122,457	06-1992	Reim et al.	435/69.1
*	B	US-4,772,547	09-1988	Heimer et al.	435/5
*	C	US-4,963,532	10-1990	Carter, William A.	514/44R
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)			
*	U	Sommer and Tautz, "Minimal homology requirements for PCR primers," Nucleic Acids Research, vol. 17, No. 16, 1989, page 6749.			
	V				
	W				
	X				

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.	Confirmation No. 5814
Application No.: 11/108,233	Group Art Unit: 1634
Filed: April 18, 2005	Examiner: Bradley L. Sisson
Title: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1	

November 21, 2012

Mail Stop Amendment
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

RESPONSE

Sir:

This is responsive to the July 23, 2012 Office Action issued regarding the above-referenced patent application. Please enter the following amendments and consider the following remarks.

If any extension of time for the accompanying response or submission is required, Applicants request that this be considered a petition therefor. The Commissioner is hereby authorized to charge any additional fee, which may be required, or credit any refund, to our Deposit Account No. 50-0220.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 8 of this paper.

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-35. (canceled)

36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer is a maximum of 50 nucleotides in length and comprises

(1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably linked to said first oligonucleotide; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

37. (canceled)

38. (previously presented) The pair of oligonucleotide primers of claim 36, wherein the promoter is a T7 promoter, a T3 promoter, or an SP6 promoter.

39-40. (canceled)

41. (currently amended) A primer set for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said set consisting of a first primer and a second primer, wherein said first primer is a maximum of 50 nucleotides in length and comprises:

(1) a first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably linked to said first hybridizing oligonucleotide; and wherein said second primer comprises a second hybridizing oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

42. (previously presented) The primer set of claim 41, wherein the promoter is selected from the group consisting of a T3 promoter, a T7 promoter and an SP6 promoter.

43-45. (canceled)

46. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer is a maximum of 50 nucleotides in length and comprises

(1) a first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length, wherein said first hybridizing oligonucleotide comprises at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a non-hybridizing promoter operably linked to said hybridizing oligonucleotide; and wherein said second primer comprises a second hybridizing oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length, wherein said second hybridizing oligonucleotide comprises at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

47. (canceled)

48. (previously presented) The pair of oligonucleotide primers of claim 46, wherein said nonhybridizing promoter comprises a T7 promoter, a T3 promoter, or an SP6 promoter.

49. (canceled)

50. (withdrawn) A test kit for the detection of HIV-1 nucleic acid in a sample comprising:

- a) the pair of oligonucleotide primers of any one of claims 36, 41, and 46; and
- b) one or more detectably labeled oligonucleotides comprising a nucleic acid sequence substantially complementary to at least part of the target sequence produced in an amplification reaction comprising the pair of oligonucleotide primers of (a).

51. (canceled)

52. (withdrawn) A method for the detection of HIV-1 nucleic acid in a sample, comprising:

- a) contacting the sample with the pair of oligonucleotide primers of claim 36 under conditions whereby nucleic acid amplification can occur; and
- b) detecting the presence of amplified HIV-1 nucleic acid, thereby detecting HIV-1 nucleic acid in the sample.

53. (withdrawn) A method for the detection of HIV-1 nucleic acid in a sample, comprising:

- a) contacting the sample with the primer set of claim 41 under conditions whereby nucleic acid amplification can occur; and
- b) detecting the presence of amplified HIV-1 nucleic acid, thereby detecting HIV-1 nucleic acid in the sample.

54. (canceled)

55. (withdrawn) A method for the detection of HIV-1 nucleic acid in a sample, comprising:

- a) contacting the sample with the pair of oligonucleotide primers of claim 46 under conditions whereby nucleic acid amplification can occur; and
- b) detecting the presence of amplified HIV-1 nucleic acid, thereby detecting HIV-1 nucleic acid in the sample.

56. (withdrawn) A method for amplifying HIV-1 nucleic acid in a sample, comprising contacting the sample with the pair of oligonucleotide primers of any one of claims 36, 41, and 46 under conditions whereby an amplification reaction can occur.

57. (canceled)

58. (currently amended) The pair of oligonucleotide primers of claim 36, wherein said first oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

said second oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

59. (currently amended) The primer set of claim 41, wherein said first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

said second hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

60. (currently amended) The pair of oligonucleotide primers of claim 46, wherein said first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

said second hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

61. (canceled)

REMARKS

Upon entry of the foregoing amendment, claims 36, 38, 41, 42, 46, 48, 50, 52, 53, 55, 56, and 58-60 are pending in the application, with 36, 41, and 46 being the independent claims. Claims 50, 52, 53, 55, and 56 have been withdrawn by the Examiner as being directed to a non-elected invention. Claim 61 has been canceled without prejudice or disclaimer. Claims 36, 41, 46, and 58-60 have been amended to claim the invention with more particularity. Support for the amendments is found in the specification *inter alia* at page 5, lines 17-28, page 6, lines 8-10, and page 7, line 31 to page 8, line 1. No new matter has been added.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Withdrawal of Finality

Applicants appreciate the withdrawal of finality by the Examiner and the issuance of a non-final Office Action.

Rejections Under 35 U.S.C. § 101

Claims 36, 38, 41, 42, 46, 48, and 58-61 have been rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. (Office Action, page 3). Applicants respectfully traverse this rejection.

The Examiner states that the primers pairs of the present invention are claimed in such general terms that the claims fairly encompass embodiments that are not only known, but also seek to block future development in the area of art. (Office Action, pages 6-7). The Examiner concludes that the claims are deemed to focus on the natural laws and do not “also contain other elements or a combination of elements . . . [so] to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself.” (Office Action, page 7).

Applicants respectfully disagree. Claim 61 has been canceled, rendering that portion of the rejection moot. The USPTO recently issued the *2012 Interim Procedure for Subject Matter Eligibility Analysis of Process Claims Involving Laws of Nature* setting forth the procedure for determining the subject matter eligibility of claims based on *Mayo v. Prometheus* (566 U.S. ____ (2012)). The first step in the procedure is to determine whether the claims are directed to a process.

If they are not, the analysis does not apply to the claims. Here, the rejected claims are all product claims directed to primer pairs. Thus, the claims are subject matter eligible under *Mayo* and the rejection is improper.

Applicants respectfully request that the rejection of claims 36, 38, 41, 42, 46, 48, and 58-61 under 35 U.S.C. § 101 be withdrawn.

Rejections Under 35 U.S.C. § 112

Claims 36, 38, 41, 42, 46, 48, and 58-61 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. (Office Action, page 7). Applicants respectfully traverse this rejection.

The Examiner states that the primers/hybridizing oligonucleotides can be 26 nucleotides in length but, in the case of the first oligonucleotide, the molecule is to also “comprise” any desired “promoter,” be it known or not. (Office Action, pages 8-9). The Examiner further states that the term “a” has been construed to encompass any and all variants of the T7, T3, and SP6 promoters, be it known or unknown, and be it naturally occurring and/or the result of genetic manipulation. (Office Action, page 9). The Examiner alleges that Reim *et al.* (US Patent No. 5,122,457, (hereinafter “Reim”)) teaches of there being a variety of T7 promoters in at least three classes and that a T7 promoter they isolated is 1136 nucleotides in length. (Office Action, page 9). The Examiner states the “first primer,” which comprises a first oligonucleotide and a promoter, is actually in excess of 1140-1160 nucleotides. (Office Action, page 9).

Applicants respectfully disagree. Claim 61 has been canceled, rendering that portion of the rejection moot.

Applicants have discovered a pair of primer binding sites in the HIV-1 LTR that, when targeted by primers having SEQ ID NOS: 1 and 5 in an amplification reaction, can be used to identify all strains of HIV-1 known at the time the invention was made. The present claims are directed to a genus of primer pairs wherein each member of the primer pair encompasses a substantial portion of SEQ ID NOS: 1 and 5, respectively. Thus, each of the primer pairs will amplify the same region of the LTR amplified by primers having SEQ ID NOS: 1 and 5. Because each member of the genus of primers pairs encompassed by the present claims contains the structural feature of a substantial portion of SEQ ID NOS: 1 and 5 and amplifies the same region of

the LTR amplified by primers having SEQ ID NOS: 1 and 5 shown to be useful to identify all strains of HIV-1 known at the time the invention was made, the genus is adequately described.

The claims as amended are directed in part to a first primer that is a maximum of 50 nucleotides in length. The first oligonucleotide and promoter that are comprised within the first primer therefore are limited in length such that the first primer is no longer than 50 nucleotides. As the first oligonucleotide must contain at least 10 sequential nucleotides of SEQ NO: 1, the promoter can be no longer than 40 nucleotides maximum. The Examiner referral to a T7 promoter 1136 nucleotides in length as allegedly disclosed in Reim is therefore irrelevant to the present claims as such a promoter is not encompassed by the present claims.

It is further noted that Reim in fact does not disclose a T7 promoter that is 1136 nucleotides in length. What Reim actually discloses is an isolated 1136 nucleotide fragment of the T7 genome containing the carboxy terminal end of the T7 RNA polymerase gene and "encompassing the T7 RNA polymerase 1.1A promoter" (column 12, lines 40-53). In other words, Reim describes a genomic fragment of T7 that contains within it the 1.1A promoter. Reim does not state or even suggest that the 1.1A promoter makes up the entire isolated fragment. Thus, the Examiner is incorrect in stating that the promoter is 1136 nucleotides in length.

Because the first primer of the present claims has a maximum length of 50 nucleotides and the first oligonucleotide has a length of 10-26 nucleotides, the promoter can have a length of 24-40 nucleotides. Thus, the Examiner's assertion that the claims are construed to encompass any and all variants of the T7, T3, and SP6 promoters is not accurate. The promoter is restricted to the length requirements recited in the claims. Further, the Examiner's discussion of a first primer having a length of 1140-1160 nucleotides is irrelevant as the first primer is limited to a maximum length of 50 nucleotides.

Using the first primer as an example, the Examiner states that the claims do not specify the nucleotide sequence for those residues that are not found in SEQ ID NO:1 and that when each of the common four nucleotides are substituted for each of the possible positions for just one terminus, there are some 5,726,623,060 possible different oligonucleotides to choose from. (Office Action, page 9). The Examiner further states that the same holds true for the other terminus as well as for both termini of the primer and that, ignoring the genera of promoter sequences encompassed by the claims, the claims encompass a genus of some 22.9 billion oligonucleotides. (Office Action, page

9). The Examiner notes that the specification discloses 14 different sequences, of which SEQ ID NOS: 1 and 5 are included. (Office Action, page 9).

Applicants respectfully disagree. As amended, the claims are directed in part to a first oligonucleotide which is fully complementary to a primer binding site in the HIV-1 LTR. Of the 10-26 nucleotides in the first oligonucleotide, at least 10 sequential nucleotides are from SEQ ID NO: 1. Because the entire first oligonucleotide is complementary to primer binding site in the LTR sequence, the nucleotide sequence for those residues that are not found in SEQ ID NO: 1 cannot be any random nucleotide as stated by the Examiner. The residues are limited to those nucleotides that are complementary to a HIV-1 LTR sequence. The calculations performed by the Examiner to determine the size of the genus is based on the substitution of the four common nucleotides at each possible position. These calculations are irrelevant to the present claims because each position is not open to any of the four common nucleotides, it is limited to the nucleotide that is complementary to a primer binding site in the LTR sequence. The same is true for the claimed second oligonucleotide, which is fully complementary to a primer binding site in the HIV-1 LTR.

As stated in MPEP 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. *See Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). Here the specification describes through actual reduction to practice three different sequences (SEQ ID NOS: 1-3) that are encompassed by the claimed first oligonucleotide and one sequence (SEQ ID NO: 5) encompassed by the claimed second oligonucleotide.¹ The specification further describes primers by a structural property (a substantial portion of SEQ ID NOS: 1 and 5) coupled with a disclosed correlation between that structure and a function (the ability to recognize all strains of HIV-1 known at the time the invention was made). Between the actual reduction to practice and the disclosed identifying

¹ It is noted that SEQ ID NO: 4 is also very similar to the claimed second oligonucleotide as it contains 9 sequential nucleotides from SEQ ID NO:5.

characteristics, the specification clearly provides an adequate written description of the claimed genus of primer pairs.

The Examiner states that the conditions for hybridization are limited only in that “nucleic acid amplification can occur” and that such language has been construed as encompassing any level of amplification, including less than specific amplification. (Office Action, page 10). The Examiner further states that, although the claims recite the limitation that the primers are to be useful in the amplification of the LTR of HIV-1, there is no requirement that they actually bind to the LTR of any HIV-1. (Office Action, page 10). The Examiner alleges that, because the genome of HIV-1 contains a LTR at both ends, any primer that anneals to any region of the genome of HIV-1, be it within the LTR or not, and be it to a conserved region or not, will ultimately result in amplification of the LTR if the primer extension reaction is allowed to go to completion – the end of the HIV-1 genome/nucleotide sequence. (Office Action, page 10). The Examiner cites Sommer and Tautz, *Nucleic Acids Res.* 17:6749 (1989) to allege that effective priming can occur where only two or three nucleotides of the 3' terminus binds. (Office Action, page 10).

Applicants respectfully disagree. The claims are directed to a set of primers that amplify a target sequence between two primer binding sites in the HIV-1 LTR region. The claims recite that the primers are fully complementary to a primer binding site in the LTR region and bind thereto in conditions under which nucleic acid amplification can occur. The claims further recite that the primers amplify the target sequence between the two primer binding sites in conditions under which nucleic acid amplification can occur. The claims require that the primers actually bind to the LTR of a HIV-1 genome. The claims further require that the primers be capable of amplifying the target sequence between the two primer binding sites. Thus, the claims do not read on any primer that anneals to any region of the genome of HIV-1. Primers that simply amplify the entire LTR do not meet the requirements of the claims.

The Examiner states that the claims fairly encompass embodiments where some 16 consecutive nucleotides do not need to be complementary to SEQ ID NOS: 1 and/or 5 and do not need to be complementary to any HIV-1 LTR. (Office Action, page 10).

Applicants respectfully disagree. The claims as amended require that the primer be fully complementary to a sequence of the HIV-1 LTR at a primer binding site.

The Examiner states that the claims fairly encompass nucleotides that will hybridize to any region of any isolate of HIV-1, be it known at the time of filing or yet to be discovered and that the first primer also comprises a promoter which has been construed as encompassing not only any promoter known at the time of filing, but also those that have yet to be discovered. (Office Action, page 11). The Examiner alleges that the disclosure of two sequences has not been found to satisfy the written description requirement. (Office Action, page 11).

Applicants respectfully disagree. The written description requirement of 35 U.S.C. § 112, first paragraph, is met if the specification describes the invention in sufficient detail to reasonably convey to one of skill in the art that the inventor had possession of the claimed invention (*Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (en banc)). Nowhere in 35 U.S.C. § 112, first paragraph, or in the written description guidelines promulgated by the USPTO is it stated that the specification must describe future embodiments that have yet to be discovered. Thus, the Examiner's reference to isolates of HIV-1 and promoters that have yet to be discovered is irrelevant to the adequacy of the written description of the present invention.

While the Examiner states that the disclosure of two sequences has not been found to satisfy the written description requirement, Applicants respectfully point out that the disclosure of a representative number of species is not the only means by which a genus can be adequately described. A genus also can be identified by its relevant identifying characteristics (*In re Alonzo*, 88 USPQ2d 1849, 1852 (Fed. Cir. 2008)). Here the specification describes through actual reduction to practice three different sequences (SEQ ID NOS: 1-3) that are encompassed by the claimed first oligonucleotide and one sequence (SEQ ID NO: 5) encompassed by the claimed second oligonucleotide. The specification further describes primers by a structural property (a substantial portion of SEQ ID NOS: 1 and 5) coupled with a disclosed correlation between that structure and a function (the ability to recognize all strains of HIV-1 known at the time the invention was made). Between the actual reduction to practice and the disclosed identifying characteristics, the specification clearly provides an adequate written description of the claimed genus of primer pairs.

Furthermore, Applicants respectfully assert that the disclosed primer sequences are a representative number of species of the claimed genus. Because each of the claimed first and second primers must comprise a substantial portion of SEQ ID NOS: 1 and 5, respectively, must be fully complementary to a primer binding site in a HIV-1 LTR, and is limited in length, the genus is

not overly large and each of the species within the genus has tremendous structural similarity. Thus, a single primer pair is representative of the entire genus.

In response to Applicants' arguments in the response filed May 9, 2012, the Examiner states that the claims fairly encompass oligonucleotides that hybridize under any conditions to the target and that the useful primers are to be selected from a genus that numbers in the tens of billions. (Office Action, page 12). The Examiner further states that the claims do not require that the portion of the primer that is actually responsible for priming be conserved at all and that the claims encompass primers that will hybridize to any nucleotide sequence that can be found somewhere in HIV-1 and any other source of DNA. (Office Action, page 12). The Examiner notes that any primer that hybridizes at any point of a HIV-1 genome will result in amplification of LTR sequences and that, given such lack of specificity, one would have no expectation that any "superior results" or even useful results would be obtained. (Office Action, page 12).

Applicants respectfully disagree. As described above, the genus of primers does not number in the tens of billions. Because each of the claimed first and second primers must comprise a substantial portion of SEQ ID NOS: 1 and 5, respectively, must be fully complementary to a primer binding site in a HIV-1 LTR, and is limited in length, the genus is not overly large. The claims require that the portion of the primer responsible for priming be fully complementary to a primer binding site in the LTR. The claims do not encompass primers that will hybridize to any nucleotide sequence that can be found in any source of DNA in addition to HIV-1. Given the narrow genus encompassed by the claims, it is clear that each species within the genus would be useful to detect HIV-1.

The Examiner acknowledges that primer sets that are incapable of amplifying the target are not encompassed within the scope of the claims, but states that the claims do not exclude any primer that is also capable of binding to non-conserved nucleotide sequences such as is found in any number of diverse sources. (Office Action, pages 12-13). The Examiner alleges that there is a lack of adequate description of those primers that are useful from those that are not so as to reasonably suggest that Applicants had possession of the full genus of useful primers when one is forced to select from tens of billions of candidate primers. (Office Action, page 13).

Applicants respectfully disagree. As described above, the claimed primers are fully complementary to a primer binding site in the HIV-1 LTR. The genus of the present claims does

not contain tens of billions of candidate primers. The genus is directed solely to primers that comprise substantial portions of the nucleotide sequence of SEQ ID NOS: 1 and 5 and are fully complementary to a primer binding site in the HIV-1 LTR, and therefore are clearly useful for the detection of HIV-1. The skilled artisan does not have to select from members of the claimed genus to identify those that are useful because all of the primers in the narrow genus encompassed by the claims are useful. Thus, the claims are adequately described.

The Examiner states that the claims are not drawn to a method of making probes but rather to the probes themselves, and Applicants' arguments regarding the ability of the skilled artisan to develop useful probes is an attempt to satisfy the written description requirement through obviousness. (Office Action, page 13).

Applicants respectfully disagree as the Examiner has misunderstood Applicants' argument raised in the previous response. Applicants did not argue that the skilled artisan would be able to "develop" useful probes. Rather, Applicants argument is that there is adequate disclosure of the claimed primer sets for one of skill in the art to produce functional primers. That is not an argument for obviousness.

Applicants respectfully request that the rejection of claims 36, 38, 41, 42, 46, 48, and 58-61 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 36, 38, 41, 42, 46, 48, and 58-61 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Montagnier *et al.* (U.S. Patent No. 5,221,610, hereafter "Montagnier") in view of Applicants' alleged admissions. (Office Action, page 14). Applicants respectfully traverse this rejection.

The Examiner alleges that Applicants have made an admission in the specification that the *env* gene of HIV has higher sequence variation between subtypes than other regions. (Office Action, pages 17-18). The Examiner states that Montagnier teaches explicitly of preparing primers specific for HIV and that these primers are to be "derived from highly conserved regions of the viral genome, such as the LTR . . ." (Office Action, page 18). The Examiner is of the opinion that, given the state of the art and the explicit guidance to identify primers in this very region, one would have

been amply motivated and would have also had a most reasonable expectation of success. (Office Action, page 18).

Applicants respectfully disagree. Claim 61 has been canceled, rendering that portion of the rejection moot.

The United States Supreme Court has articulated that obviousness under § 103(a) is determined by an analysis of the following factors: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The obviousness or nonobviousness of the subject matter is to be determined based on these considerations, however, secondary considerations such as commercial success, long-felt but unresolved needs and the failure of others can be utilized to determine the circumstances surrounding the origin of the invention. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1730 (2007). If such secondary considerations exist, they must be considered. *See Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538-1539 (Fed. Cir. 1983).

In *KSR*, the Supreme Court also made clear that predictable variations are likely obvious, but unpredictable variations are not:

If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative - a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

KSR at 1740.

The Court also recognized that when the prior art taught away from the claimed invention, the invention was more likely to be non-obvious: "when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR* at 1740 (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1996)).

The Court also emphasized the importance of identifying "a reason" that a person of ordinary skill in the relevant field would have combined the elements in the fashion claimed by the

new invention. *Id.* at 1731. The Court also emphasized that this analysis should be made explicit:

Often it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit.

Id. at 1740-1741 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

Claim 36 is representative of the present invention.

36. A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer is a maximum of 50 nucleotides in length and comprises

(1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably linked to said first oligonucleotide; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

Applicants assert that Montagnier does not explicitly point to the development of primers targeted to the LTR. The sentence that the Examiner quotes from Montagnier must be considered for all it teaches, not just the portion of the sentence highlighted by the Examiner. The cited sentence in full states that “[f]or this reason, the PCR technique is preferably carried out with several primer pairs and probes derived from highly conserved regions of the viral genome, such as the LTR, qao [sic, gag], and env regions of HIV-1.” (column 19, line 67 to column 20, line 2). Thus, Montagnier does not specifically point to the LTR as the Examiner asserts, it directs one to use any highly conserved region of the viral genome, and provides the LTR, gag, and env regions as examples. The sentence in Montagnier, which is the only mention in the patent of primers directed to conserved regions, would be interpreted by one of ordinary skill in the art to impart two teachings: (1) that any highly conserved region anywhere in the HIV-1 genome is likely to be effective; and (2) that highly conserved regions may be found in the LTR, gag, and env regions, which make up more than 50% of the genome of HIV-1. Because Montagnier points to regions making up more than half of the genome and does not single out the LTR over the other listed regions or any other highly conserved region, the Examiner overstates the relevancy of the teaching of Montagnier when the Examiner asserts that Montagnier provides “explicit guidance to identify primers in this very region.” (Office Action, page 18).

The Examiner states that the above argument is not persuasive because the env gene was known in the art to be the most variable of all the genes, which reasonably implies that the LTR is more conserved. (Office Action, page 18). The Examiner concludes that one of ordinary skill in the art would have been motivated to choose that part of the HIV genome that is not subject to such high variability in the selection of primers from highly conserved regions. (Office Action, pages 18-19).

Applicants respectfully disagree. The Examiner’s reasoning regarding the variability of the env gene and the selection of primers is flawed. Even if the env gene is the region of the HIV-1 genome with the highest variability, one of ordinary skill in the art was aware that the env gene contained conserved sequences. This is apparent from the references disclosed in the present specification and discussed by the Examiner. In the sentences regarding env gene variability in the specification that are quoted by the Examiner (starting at page 2, line 13), the specification refers to a study by McCutchan *et al.* (*J. AIDS* 4:1241(1991)) in which “primers were chosen from relatively

conserved regions in gag, env and LTR” (page 2, lines 18-20). In the paragraph quoted by the Examiner beginning on page 2, line 33, the specification cites another study (Engelbrecht *et al.*, *J. Virol. Meth.* 55:391 (1995)) on the development of an assay “using env, gag and LTR primer pairs to detect subtypes in the Western Cape, South Africa.” These cited references provide evidence that one of ordinary skill in the art was aware of conserved sequences within the env gene and actively sought to develop primers directed to those conserved sequences. Thus, the Examiner’s conclusion that one would not choose to develop primers from the env gene because of the alleged high variability in the env gene is incorrect.

The Examiner acknowledges that Montagnier does not teach primers having the claimed sequences SEQ ID NO:1 or SEQ ID NO:5 but states that Applicants teach in the specification how these sequences are highly conserved in HIV. (Office Action, page 19). The Examiner is of the opinion that it would have been obvious to select these sequences as well as the claimed oligonucleotide length based on the explicit guidance by Montagnier to select just such highly conserved sequences. (Office Action, page 19).

Applicants respectfully disagree. As stated above, the single sentence in Montagnier regarding primer pairs directed to highly conserved regions suggests at most that any highly conserved region in the genome will be sufficient to detect HIV-1 variants. As the Examiner acknowledges, Montagnier does not disclose primers comprising SEQ ID NO:1 or SEQ ID NO:5. The Examiner’s conclusion that it would have been obvious to select primers comprising SEQ ID NO:1 or SEQ ID NO:5 because the present specification teaches that these sequences are highly conserved in HIV is an egregious example of hindsight reasoning by the Examiner. The Examiner’s reasoning appears to be that Montagnier suggests using any conserved HIV sequence, the specification discloses such a sequence, so one of ordinary skill in the art would have picked the disclosed sequence. This reasoning is improper for an obviousness analysis. The genome of HIV-1 is replete with highly conserved regions as acknowledged by Montagnier, which points to the LTR, gag, and env regions as examples of sections of the HIV-1 genome that contain such conserved regions. Nothing in Montagnier directs one of ordinary skill in the art to select SEQ ID NO:1 or SEQ ID NO:5 out of all of the potential conserved regions in the genome. The only guidance pointed to by the Examiner to lead one to the claimed sequences is the teaching of the present specification. This is clearly improper.

The Examiner states that the present claims are directed to a composition of primers, not a method, and the claims do not prohibit the combining of the resultant primer pairs with other primer pairs in a multiplex reaction. (Office Action, page 19). The Examiner therefore concludes that the fact that Montagnier teaches combining primers to detect variants of HIV-1 because a single primer pair may not produce reliable results does not overcome the alleged obviousness of the claimed primer sets.

Applicants respectfully disagree. Montagnier teaches that any single primer pair may not produce reliable results due to genetic variations or deletions in the regions targeted for amplification and therefore teaches that it is preferred to carry out amplification with several primer pairs (column 19, line 60 to column 20, line 2). Thus, one of ordinary skill in the art reading Montagnier would understand that no single primer pair would detect most or all variants of HIV-1. In contrast, the presently claimed primer pairs are capable of detecting all HIV-1 variants tested in the disclosed examples. Thus, the presently claimed invention provides superior results that obviate the need for multiple primer pairs as taught by Montagnier. As Montagnier provides no teaching or suggestion that primer pairs having this ability are possible, it cannot render the present claims obvious. While the Examiner suggests that the claimed primer pairs can be combined with other primer pairs for use in a multiplex amplification reaction, the fact is that the claimed primer pairs have superior properties that overcome the need for a multiplex amplification, a fact that could not have been predicted by one of ordinary skill in the art based on a reading of Montagnier. For at least this reason, the claimed invention is non-obvious.

The Examiner further alleges that Applicants admit that promoter-primers are known in the art. (Office Action, page 20). The Examiner is of the opinion that one of ordinary skill in the art would have been motivated to include promoters on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences. (Office Action, page 21).

Applicants respectfully disagree. The claimed primer sequences are non-obvious for at least the reasons discussed above. Any alleged knowledge of the use of promoter-primers would not render the claimed invention obvious as the primers themselves remain non-obvious.

The Examiner states that the LTR is less than 1 kb in size and that, given such a small target area, and specific guidance as to where and what to be looking for, there exists but a finite number

of identified, predictable solutions as there exists but a finite number of highly conserved regions with the LTR of HIV. (Office Action, page 22).

Applicants respectfully disagree. As stated above, Montagnier does not direct one of ordinary skill in the art to the LTR region specifically, it directs one to any highly conserved region in the HIV-1 genome. At a minimum, this includes the LTR, gag, and env regions of the genome as stated by Montagnier. The LTR has a length of about 640 base pairs, while the gag and env genes have a length of about 1500 and 2570 base pairs, respectively. These three regions (including both LTRs) add up to a total of about 5330 base pairs, more than 50% of the total HIV-1 genome. Even if one were to limit a search to the LTR, gag, and env regions based on the disclosure of Montagnier, more than half the genome would still have to be searched for highly conserved sequences. Thus, one of ordinary skill in the art has not been “[g]iven such a small target area” as suggested by the Examiner. Furthermore, Montagnier does not provide any “specific guidance as to where and what to be looking for” as suggested by the Examiner. Montagnier provides no specific guidance at all in the one sentence disclosure regarding conserved sequences. In particular, Montagnier provides absolutely no guidance on what to look for, *e.g.*, no definition of “highly conserved.” Furthermore the Examiner fails to support his statement that “there exists but a finite number of ‘highly conserved’ regions with the LTR of HIV” with any evidence other than the total length of the LTR. Given the large target area disclosed in Montagnier and the total lack of guidance as to what to look for, there clearly is more than a finite number of identified, predictable solutions. For at least this reason, the claimed invention is non-obvious.

In response to Applicants’ previous arguments regarding the Examiner’s improper use of a statement in the specification as a prior art admission, the Examiner alleges that the absence in the specification of a label of a section as prior art does not shield applicants from prior art statements being used as such and that the Examiner has provided underlying facts and reasoning to support the conclusion that the statement is a prior art admission. (Office Action, page 23).

Applicants respectfully disagree. In the Office Action mailed January 9, 2012, the Examiner alleged that the statement in the present specification that “[s]ensitive assays are therefore needed that are capable of detecting as much variants of the HIV-1 virus as possible (preferably all)” qualifies as an admission of prior art by Applicants. In that Office Action, the Examiner failed to set forth any underlying facts and reasoning leading to the conclusion that the statement constitutes

a prior art admission as required by the Board of Patent Appeals and Interferences (BPAI) (*see In re Shirley*, Appeal 2009-2352, pages 22-23). Yet, in the present Office Action, the Examiner states that underlying facts and reasoning have been provided without pointing to any such facts and reasoning. (Office Action, page 23). Further the Examiner has failed to address *In re Burdgick* (Appeal 2009-004835, page 6) discussed in the previous response, which holds that a statement of need in the art is not an admission of prior art. Thus, Applicants assert that the statement in the specification regarding the need for an assay to detect variants of HIV-1 is not an admission of prior art and cannot be relied on as the basis for an obviousness rejection.

In response to Applicants' previous arguments, the Examiner alleges that hindsight reasoning was not used because the rejection clearly sets out specific publications which Applicants allegedly admit disclose methods not only for selecting primers for HIV, but also the need for being able to detect the many variants of HIV. (Office Action, pages 23-24). The Examiner further states that the rejection clearly sets out that it was known in the art years prior to the effective filing date that the env gene of HIV-1 was the most variable region of the HIV-1 genome. (Office Action, page 24).

Applicants respectfully disagree. As stated above, Applicants assert that no admission of prior art has been made regarding the need for being able to detect variants of HIV. Also as stated above, the statements by the Examiner regarding alleged admissions about the variability of the env gene are irrelevant when the exact same references disclose that primers targeted to conserved sequences of the env gene were developed. The Examiner has not provided any teachings or reasoning why one of ordinary skill in the art would select the specifically claimed primer sequences other than the statement that the present specification discloses the sequences. The only art cited by the Examiner (Montagnier) suggests targeting conserved sequences anywhere in the HIV genome, not only the LTR and certainly not the specific sequences within the LTR that are presently claimed. The disclosure in the present specification of the variability of the env gene, even if it were an admission of prior art, is not a suggestion to avoid targeting the env gene with primers when the disclosure states that primers targeting the env, gag, and LTR regions were developed. In fact, the references disclosed on page 2 of the specification provide similar teachings to Montagnier, *i.e.*, that a primer can be targeted to conserved sequences anywhere in the HIV genome. Thus, neither Montagnier nor any alleged admissions of prior art point one of ordinary

skill in the art to the specifically claimed primers. In the absence of any guidance leading one to the specifically claimed invention there can be no finding of obviousness.

In response to Applicants' previous arguments, the Examiner states that it was known in the art that the env gene was the most variable and that it stands to reason that if the env gene is the most variable, then the LTR is one of, if not the most highly conserved region. (Office Action, page 24). The Examiner alleges that, with Montagnier teaching one to produce primers that are directed to highly conserved nucleotide sequences, and then specifically identifying the LTR region, and the artisan being well aware that the env gene is highly variable, the artisan would have been amply motivated to have selected primers that are derived from those highly conserved regions of the HIV-1 LTR, which clearly speaks to the existence of a finite number of identified predictable solutions to the art-recognized problem. (Office Action, page 24).

Applicants respectfully disagree. The Examiner's statement that "it stands to reason that if the env gene was the most variable, then the LTR is one of, if not the most highly conserved region" is illogical. The Examiner has not pointed to any teaching regarding the level of variability of the HIV LTR. The Examiner has not disclosed any relationship between the variability of the env gene and the variability of the LTR or any reason why high variability in env necessarily means low variability in the LTR. The Examiner's attempt to show that one of ordinary skill would be directed specifically to the LTR region, much less the specifically claimed primers, is unsupported by evidence.

In response to Applicants' previous arguments, the Examiner states that the phrase "under conditions whereby nucleic acid amplification can occur" in the present claims has been construed as encompassing any conditions, including those where less than superior results are obtained. (Office Action, page 25). The Examiner further points to Sommer and Tautz as teaching that just two nucleotides at the 3' terminus of a primer is all that is needed in order to satisfy conditions whereby nucleic acid amplification can occur. (Office Action, page 25).

Applicants respectfully point out that the present claims are directed to primers that are fully complementary to a primer binding site in the LTR region. Thus, the argument that only two complementary nucleotides are needed for amplification is irrelevant.

For at least the reasons discussed above, the Examiner has failed to make a *prima facie* case of obviousness. Even if such a case had been made, however, the present specification discloses

unexpectedly superior results for the claimed primers that overcome any alleged obviousness of the invention.

The claimed primers exhibit unexpectedly superior results in view of any teachings in the art. Such evidence is indicative of non-obviousness and must be considered by the Office (M.P.E.P. §716.02(a)(III)). When considering the unexpected superiority of a composition, such as the claimed primer pairs, the Office needs to consider the properties of the claimed subject matter rather than just the structural similarity of the compositions with the prior art (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

The properties of the claimed primer pairs at issue are their ability to identify all subtypes of HIV-1 known at the time the invention was made. As discussed above, the claimed primer pairs are superior to any primer pairs taught or suggested in the cited art because the use of these primer pairs in assays for the detection of HIV-1 allows the detection of all subtypes of HIV-1 tested. The properties of the claimed primer pairs are also unexpected in view of Montagnier because this reference suggested that any of the conserved regions of the HIV-1 genome, such as the LTR, env and gag regions, could be used for detecting HIV-1. As evidenced by the data set forth in Table 2 of Example 3; Table 3 of Example 4; and Table 4 of Example 5 of the present specification, the primer pairs of the present invention detected all subtypes of HIV-1 tested, while those prepared from a conserved sequence within the gag region were not able to do so. Thus, the primer pairs of the present invention provide superior results with regard to the use of a single primer pair for detection of all subtypes of HIV-1. This result could not have been predicted based on the cited art or on what was known in the art generally at the time the present application was filed.

Applicants respectfully request that the rejection of claims 36, 38, 41, 42, 46, 48, and 58-61 under 35 U.S.C. § 103(a) be withdrawn.

Rejoinder of method claims

Applicants further specifically request that claims 50, 52, 53, 55, and 56 be rejoined and examined in the present application, once a determination is made that the composition claims under examination are allowable. Specifically, if the composition claims 36, 38, 41, 42, 46, 48, and 58-60 are found to be allowable, applicants request that the Examiner review and examine claims 50, 52, 53, 55, and 56, which depend from these composition claims, according to the practice of

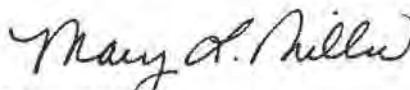
rejoinder as set forth in section 821.04 of the MPEP. In particular, it is stated therein that if a product claim is elected in a restriction and then found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim are to be rejoined.

CONCLUSION

Accordingly, Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any small matters outstanding of resolution, he is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

No fee other than those accompanying this response is believed to be due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



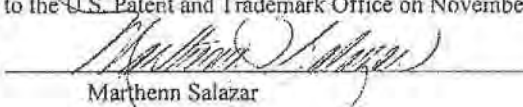
Mary L. Miller
Registration No. 39,303

Customer Number 20792
Myers Bigel Sibley & Sajovec, P.A.
P.O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on November 21, 2012.

Signature: _____



Marthenn Salazar

Electronic Acknowledgement Receipt

EFS ID:	14287163
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Mary L. Miller/Martheinn Salazar
Filer Authorized By:	Mary L. Miller
Attorney Docket Number:	9310-22CT
Receipt Date:	21-NOV-2012
Filing Date:	18-APR-2005
Time Stamp:	11:47:08
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Extension of Time	9310-22CT_EOT.pdf	51709 342e124f548b8bec13816ae341bc8adb3e58e2156	no	1

Warnings:

Information:

2		9310-22CT_Response.pdf	1131367	yes	25
			29a0b93af5bb33e33bf007e501a7c0538202bf3		
Multipart Description/PDF files in .zip description					
Document Description			Start	End	
Amendment/Req. Reconsideration-After Non-Final Reject			1	1	
Claims			2	7	
Applicant Arguments/Remarks Made in an Amendment			8	25	
Warnings:					
Information:					
Total Files Size (in bytes):			1183076		
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.					

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)		Docket Number (Optional) 9310-22CT
Application Number 11/108,233	Filed April 18, 2005	
For NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1		
Art Unit 1634	Examiner Bradley L. Sisson	

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	<u>Fee</u>	<u>Small Entity Fee</u>	
☒ One month (37 CFR 1.17(a)(1))	\$150	\$75	\$ <u>150.00</u>
☐ Two months (37 CFR 1.17(a)(2))	\$570	\$285	\$ _____
☐ Three months (37 CFR 1.17(a)(3))	\$1,290	\$645	\$ _____
☐ Four months (37 CFR 1.17(a)(4))	\$2,010	\$1,005	\$ _____
☐ Five months (37 CFR 1.17(a)(5))	\$2,730	\$1,365	\$ _____

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

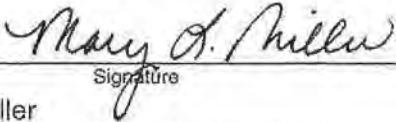
☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to
Deposit Account Number 50-0220

☐ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. 37 CFR 3.73(b) statement is enclosed (Form PTO/SB/96).
- ☒ attorney or agent of record. Registration number 39,303
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number _____

 _____ Signature	<u>November 21, 2012</u> _____ Date
<u>Mary L. Miller</u> _____ Typed or printed name	<u>919-854-1400</u> _____ Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☒ * Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Electronic Patent Application Fee Transmittal

Application Number:	11108233			
Filing Date:	18-Apr-2005			
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1			
First Named Inventor/Applicant Name:	Jaap Goudsmit			
Filer:	Mary L. Miller/Marthenn Salazar			
Attorney Docket Number:	9310-22CT			
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 1 month with \$0 paid	1251	1	150	150

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Total in USD (\$)				150

Electronic Acknowledgement Receipt

EFS ID:	14287220
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Mary L. Miller/Martheinn Salazar
Filer Authorized By:	Mary L. Miller
Attorney Docket Number:	9310-22CT
Receipt Date:	21-NOV-2012
Filing Date:	18-APR-2005
Time Stamp:	11:49:46
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$150
RAM confirmation Number	10828
Deposit Account	500220
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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1	Fee Worksheet (SB06)	fee-info.pdf	30569	no	2
			0a5ac759389ba079911f1911ca2c9e1037259eae		
Warnings:					
Information:					
Total Files Size (in bytes):				30569	
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PATENT APPLICATION FEE DETERMINATION RECORD
Substitute for Form PTO-875

Filing Date
04/18/2005

☐ To be Mailed

OTHER THAN

(Column 2)

SMALL ENTITY ☐

OR

SMALL ENTITY

FOR	NUMBER FILED	NUMBER EXTRA	RATE (\$)	FEE (\$)	RATE (\$)	FEE (\$)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(j))	minus 20 =		X \$ =		X \$ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =		X \$ =		X \$ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).					
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))						
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL		TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2

OTHER THAN

(Column 3)

SMALL ENTITY

OR

SMALL ENTITY

AMENDMENT	11/21/2012	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)		RATE (\$)	ADDITIONAL FEE (\$)
	Total (37 CFR 1.16(i))	* 14	Minus	** 25	= 0	x \$ =		OR	x \$62=	0
	Independent (37 CFR 1.16(b))	* 4	Minus	***6	= 0	x \$ =		OR	x \$250=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

(Column 3)

AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE (\$)	ADDITIONAL FEE (\$)		RATE (\$)	ADDITIONAL FEE (\$)
	Total (37 CFR 1.16(l))	+	Minus	**	=		X \$ =		OR	X \$ =	
	Independent (37 CFR 1.16(h))	+	Minus	***	=		X \$ =		OR	X \$ =	
	☐ Application Size Fee (37 CFR 1.16(s))								OR		
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))								OR		
						TOTAL ADD'L FEE			OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/JACQUELYN WILLIAMS/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814
20792 7590 02/01/2013 MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			EXAMINER SISSON, BRADLEY L	
			ART UNIT 1634	PAPER NUMBER
			MAIL DATE 02/01/2013	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

11/108,233

Applicant(s)

GOUDSMIT ET AL.

Examiner

Bradley L. Sisson

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2012.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 36,38,41,42,46,48,50,52,53,55,56 and 58-60 is/are pending in the application.
- 5a) Of the above claim(s) 50,52,53,55 and 56 is/are withdrawn from consideration.
- 6) ☒ Claim(s) 36,38,41,42,46,48 and 58-60 is/are allowed.
- 7) ☐ Claim(s) ____ is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 07 October 2011 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/463,352.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 4) ☐ Other: ____.

DETAILED ACTION

Election/Restrictions

1. Claims 50, 52, 53, 55, and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on -5 November 2007.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/463,352, filed on 21 January 2000.

Drawings

3. The drawings were received on 07 October 2011. These drawings are acceptable.

Terminal Disclaimer

4. The terminal disclaimer filed on 26 May 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent Application 11/372,577 has been reviewed and is accepted. The terminal disclaimer has been recorded.

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5. The terminal disclaimer filed on 01 May 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent 6,881,537 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112

6. The following is a quotation of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), first paragraph:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 36, 38, 41, 42, 46, 48, and 58-60 remain rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. Attention is directed to MPEP 904.01.

The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44

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USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

9. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

10. As set forth in *In re Alonso* 88 USPQ2d 1849 (Fed. Cir. 2008), at 1851:

The written description requirement of 35 U.S.C. § 112, ¶ 1, is straightforward: “The specification shall contain a written description of the invention” To satisfy this requirement, the specification must describe the invention in sufficient detail so “that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought.” *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997); see also *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 [76 USPQ2d 1724] (Fed. Cir. 2005); *Eiselstein v. Frank*, 52 F.3d 1035, 1039 [34 USPQ2d 1467] (Fed. Cir. 1995).

Alonso at 1852:

A genus can be described by disclosing: (1) a representative number of species in that genus; or (2) its “relevant identifying characteristics,” such as “complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” *Enzo*, 323 F.3d at 964.

11. Claims 36, 41 and 46 are each independent. Claim 36 is deemed representative and, for convenience, is reproduced below.

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36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer is a maximum of 50 nucleotides in length and comprises

(1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably linked to said first oligonucleotide; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

12. In applying the test as set forth in *Alonso*, it is noted that applicant is claiming compositions comprising nucleic acids that can serve as primers in the amplification of Long Terminal Repeat (LTR) sequences of any variant of HIV-1. It is noted that HIV-1 comprises two LTR regions, and that the primers are not limited as to their hybridizing to regions found in one or the other or both LTRs.

13. As presently worded, there must be two primers, with the "first primer" having a "maximum" length of 50 nucleotides. Within the 50 nucleotides is to be found both a promoter sequence.

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14. A review of the disclosure finds support for the concept of the first oligonucleotide ranging from 10 to 50 nucleotides, and that this first oligonucleotide is "operably linked to a promoter sequence," with the disclosure at page 6 specifically identifying T3, T7, and SP6.

15. A review of the disclosure fails to find where applicant contemplated the combined length of the "first primer" to not exceed 50 nucleotides in length. Accordingly, the limitations added to claims 36, 41, and 46 is deemed to constitute new matter.

16. Assuming *arguendo*, that the newly-added limitations do not constitute new matter, the disclosure still does not provide a description of any promoter that can be combined with a "first oligonucleotide" of 26 nucleotides in length of which "at least 10 sequential nucleotides of ...SEQ ID NO: 1" and not exceed the upper limit of 50 nucleotides for the complete length of the "first primer."

17. As can be seen at page 7 of the disclosure, the one embodiment exemplified by applicant shows that the T7 promoter is some 28 nucleotides in length (SEQ ID NO: 9, 10, and 11 depict SEQ ID NO:1, 2, and 3 operably linked to T7). By contrast, if one were to attempt to develop a "first primer" that comprises a "first oligonucleotide" that is 26 nucleotides in length, the promoter can be no greater than 14 nucleotides in length; however, the one example of applicant shows that T7 is some 28 nucleotides in length. Therefore, if the T7 promoter were to be operably linked to a first oligonucleotide that is 26 nucleotides in length, it would be 54 nucleotides in length ($28 + 26 = 54$), which exceeds the maximum allowable length of 50 nucleotides.

18. A review of the disclosure fails to find where applicant has satisfied either prong of the written description test as set forth in *Alonso*.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 36, 38, 41, 42, 46, 48, and 58-60 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

23. Claims 36, 41, and 46 are independent. Claim 36 is deemed representative and, for convenience, is reproduced below.

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36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer, wherein said first primer is a maximum of 50 nucleotides in length and comprises

(1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably linked to said first oligonucleotide; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

24. Attention is directed to MPEP 904.01.

The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

25. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co., Inc.*, 186 USPQ 458 (CA6

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1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

26. The claims under consideration are drawn to a composition- primers useful in the amplification of a target nucleotide sequence found within the Long Terminal Repeat (LTR) region of Human Immunodeficiency Virus Attention is directed to MPEP 2129 [R-6],

Admissions as Prior Art, which states in part:

I. ADMISSIONS BY APPLICANT CONSTITUTE PRIOR ART

A statement by an applicant >in the specification or made< during prosecution identifying the work of another as “prior art” is an admission **>which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988).

27. Attention is also directed to *Ex parte Shirley*, (BPAI, 2009) Appeal No. 2009002352, which, at pages 21 and 26, states:

The Specification’s omission of the term “prior art” and inclusion of the prior-art disclaimer may initially appear to indicate that Appellants do not consider the single-step soft bake process to constitute prior art. To place these latter, contraindicative factors into the proper context though, we note that patent-application drafters regularly endeavor to avoid the indiscriminate or imprudent use of the descriptive label, “prior art.” See *Riverwood Intern. Corp. v. R.A. Jones & Co., Inc.*, 324 F.3d 1346, 1354 (Fed. Cir. 2003) (citing *In re Fout*, 675 F.2d 297, 300 (CCPA 1982)) for the proposition that “section 102 is not the only source of ... prior art. Valid prior art may be created by the admissions of the parties”; *In re Nomiya*, 509 F.2d 566, 571 (CCPA 1975) (holding that an Applicant’s labeling of certain figures as “prior art,” *ipsissimis verbis*, constituted an admission that the pictured subject matter was prior art relative to Applicant’s invention); MPEP § 21294 (instructing that “the examiner must determine whether the subject matter identified as ‘prior art’ is applicant’s own work, or the work of another. In the absence of

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another credible explanation, examiners should treat such subject matter as the work of another”).

The Specification's omission of the term “prior art” and inclusion of the boilerplate prior-art disclaimer do not change our conclusion. In view of the record as a whole, these factors are ineffective in shielding Appellants from having their prior-art admissions treated as such.

28. Upon review of the instant disclosure it is noted that there is no part of the disclosure that is labeled as being directed to “Prior Art,” or that any of the cited documents constitute “prior art.” However, the instant disclosure has been found to specifically identify documents that were published prior to the effective filing date of the subject application. Such documents and applicant's characterization as to what they disclose are considered to be admissions as to prior art. Additionally, a review of the disclosure has also found statements by applicant as to what was known in the art at the time of the invention. Such statements are also considered to be admissions of prior art.

29. Applicant, at page 2 of the disclosure admits:

Some regions are more prone to sequence variation than others. Especially in the *env* domain sequence variation can be as high as 30% between members of the different subtypes. Ideally, primer selection should be based on knowledge of interstrain variability in candidate primer sequences and the consequences of mismatching at primer sites. McCutchan et al, J.AIDS, 4, 1241-1250, 1991, used PCR to make a genetic comparison of different HIV-1 isolates. Using anchored PCR (varying sense primers were used with a constant antisense primer, primers were chosen from relatively conserved regions in gag, env and LTR)

30. Upon review of the above statement, it is not clear if the characterization of the percent variability of the *env* gene is an admission of prior art or whether it is information obtained by

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applicant. In answering this question, it is noted that US Patent 4,772,547 (Heimer et al.), which was published nearly 9 years prior to the effective filing date of the subject application, teaches in column 5, third paragraph, that the variability of the *env* gen can be as much as 20 %.

Additionally, US Patent 4,963,532 (Carter), which issued 16 October 1990, nearly 7 years prior to the effective filing date of the subject application, states in column 1, lines 32-34: "The most variable region of the HIV genome is the envelope (*env*) gene..." In view of the state of the art at the time of filing, these statements are deemed to be admissions of prior art.

31. Applicant, at page 2, last paragraph, bridging to page 3, of the disclosure states:

Research aimed at identifying suitable primer sets for the reliable amplification of HIV-1 derived nucleic acid sequences has been ongoing for the past years. Engelbrecht et al., *J. Virol. Meth.*, 55, 391-400, 1995, describe a study aimed at the development of a specific and sensitive PCR protocol using *env*, *gag* and LTR primer pairs to detect subtypes present in the Western Cape, South Africa. Twenty four strains of which it was known that they belonged to subtypes B, C and D were analyzed.

32. Applicant, at page 3, last paragraph, admits:

Various techniques for amplifying nucleic acid are known in the art.

33. According to Montagnier, "DNA primer pairs of known sequence positioned 10-300 base pairs apart that are complementary to the plus and minus strands of the DNA to be amplified can be prepared by well-known techniques for the synthesis of oligonucleotides" (id. at col. 19, 11. 24-28). Montagnier et al., column 19, bridging to column 20, teach:

Since a patient may have been infected with HIV-1 containing genetic variations or deletions in the regions targeted for amplification, the PCR technique using a single primer pair may not produce reliable results. Specifically, such variation could result in inefficient primer or probe binding, or elimination of specific restriction endonuclease sites, or both of these problems. For this reason, the PCR technique is preferably carried

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out with several primer pairs and probes derived from highly conserved regions of the viral genome, such as the LTR, *gag*, and *env* regions of HIV-1.

Given the state of the art and the explicit guidance to identify primers in this very region, one would have been amply motivated and would have also had a most reasonable expectation of success in identifying just such primers from the finite number of possible sequences.

34. Applicant, in the response of 09 May 2012 and again in the response of 21 November 2012, presents argument that Montagnier et al., also suggests using other regions of the HIV genome in the production of primers and that as such, one would not be directed to the LTR region. This argument has been considered and has not been found persuasive. As noted above, the *env* gene was known in the art to be the most variable of all the genes. Such reasonably implies that the LTR is more conserved. Accordingly, one of ordinary skill in the art would have been motivated to choose that part of the HIV genome that is not subject to such high variability in the selection of primers from highly conserved regions. *See In re Preda*, 401 F.2d at 826 (noting that “in considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom”).

35. Montagnier et al., column 19, third paragraph, teaches that primers “can be prepared by well known techniques.”

36. Montagnier et al., has not been found to disclose SEQ ID NO: 1 or SEQ ID NO: 5; however, applicant, in the specification, teaches how these sequences are highly conserved in the LTR regions of HIV-1. Given the explicit guidance by Montagnier et al., to select just such highly conserved sequences from these very regions, the selection of sequences corresponding to

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SEQ ID NO: 1 and SEQ ID NO: 5 would have been a predictable use of prior art elements to their established functions. Further, the selection of the appropriate length would have been obvious as Montagnier et al., teaches explicitly that primers can be prepared using techniques well known in the art.

37. Applicant presents argument that Montagnier et al., teaches combining primers in a method of detecting whereas the claimed primers are to be used alone. This argument is not persuasive towards the withdrawal of the rejection as the claimed invention, for as noted above, the claims are not drawn to any method, but rather, to a composition of primers. Further, the claims do not prohibit the combining of the resultant primer pairs with other primer pairs in a multiplex amplification reaction.

38. Independent claims 36, 41, and 46 require the primers to comprise a promoter region, which in dependent claims 38, 42, and 48 is limited to "a T7 promoter, a T3 promoter, or an SP6 promoter."

39. Applicant, at page 4 of the disclosure, admits:

Another technique for the amplification of nucleic acid is the so-called transcription based amplification system (TAS). The TAS method is described in International Patent Appl. no. WO 88/10315. Transcription based amplification techniques usually comprise treating target nucleic acid with two oligonucleotides one of which comprises a promoter sequence, to generate a template including a functional promoter. Multiple copies of RNA are transcribed from said template and can serve as a basis for further amplification.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295. EP 408295 is primarily concerned with a two-enzyme transcription based amplification method. Transcription based amplification methods, such as the NASBA method as described in EP 329822, are usually employed with a set of oligonucleotides, one of which is provided with a promoter sequence that is recognized

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by a DNA dependent RNA polymerase such as, for example, T7 polymerase. Several modifications of transcription based techniques are known in the art.

In contrast to RT-PCR, NASBA, which is based on RNA transcription by T7 RNA polymerase (Kievits et al., 1991; Compton, 1991), does not need differentiation between RNA- and DNA- derived amplification products since it uses RNA as its principal target. NASBA enables specific amplification of RNA targets even in a background of DNA.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295... One or more "promoter-primers" (oligonucleotides provided with a promoter sequence) may be used in transcription based amplification techniques, optionally combined with the use of one or more oligonucleotides that are not provided with a promoter sequence. For RNA amplification, a transcription based amplification technique, is a preferred technology.

In each of the above-reproduced paragraphs, applicant has provided a summary of the disclosures of the various documents. Such statements, while not labeled as "prior art," are considered to be admissions of prior art.

40. In view of the admitted state of the art where primers comprising a promoter region, such as T7, are used in transcription-based amplification methods, and that the inclusion of the T7 promoter in such primers was known in the art, and that NASBA does not need differentiation between RNA- and DNA-derived amplification products, one of ordinary skill in the art at the time of the invention would have been motivated to have included just such a promoter on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences, be they RNA as found in the viral particles, or DNA, as is found when HIV-1 has integrated into a hosts genome (proviral sequence).

41. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007);

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When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

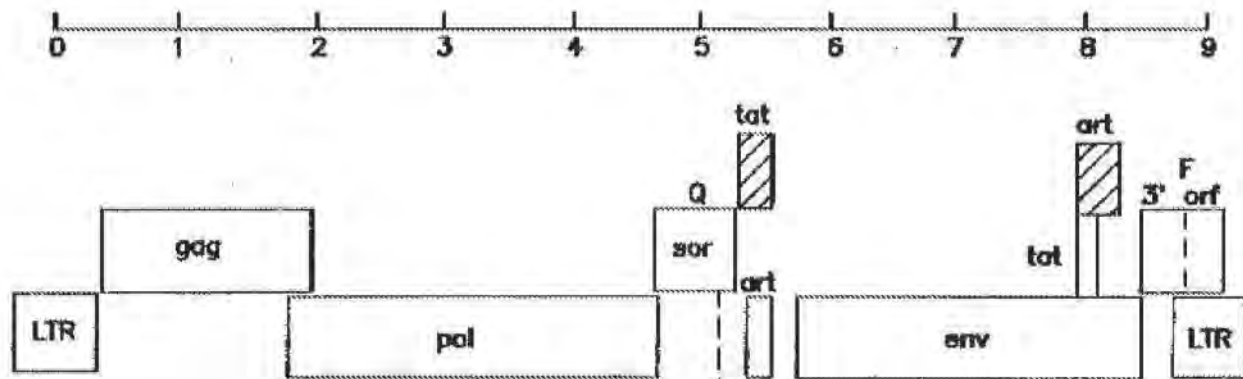
42. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes “background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR* at 1396.

43. Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

44. The prior art of record explicitly directs one to “highly conserved” regions of the HIV genome, and specifically identifies the LTR of HIV. Clearly, there exists but a finite number of “highly conserved” regions within the LTR of HIV.

45. Montagnier et al., in FIG. 1, shows that the LTR region is less than 1 kb in size.

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46. Given such a small target area, and specific guidance as to where and what to be looking for, there exists but a finite number of identified, predictable solutions. In light of the extreme interest in one being able to identify the various types of HIV, and the specific guidance provided, said ordinary artisan would have been both amply motivated and would have had a most reasonable expectation of success.

47. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-60 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

Response to argument

48. Applicant, at pages 8-17 of the response of 21 November 2012 repeats arguments traversing the rejection of claims under 35 USC 103. Special emphasis being directed to the assertion that the case at hand is not analogous to that of *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

49. Additionally, at page 11 of the response,

Applicants assert that Montagnier does not explicitly point to the development of primers targeted to the LTR. The sentence that the Examiner quotes from Montagnier must be considered for all it teaches, not just the portion of the sentence highlighted by the Examiner.

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50. Applicant, at page 12 of the response states:

The Examiner's conclusion that it would have been obvious to select primers comprising SEQ ID NO: 1 or SEQ ID NO:5 because the present specification teaches that these sequences are highly conserved in HIV is an egregious example of hindsight reasoning by the Examiner. The Examiner's reasoning appears to be that Montagnier suggests using any conserved HIV sequence, the specification discloses such a sequence, so one of ordinary skill in the art would have picked the disclosed sequence. This reasoning is improper for an obviousness analysis. The genome of HIV-1 is replete with highly conserved regions as acknowledged by Montagnier, which points to the LTR, gag, and env regions as examples of sections of the HIV-1 genome that contain such conserved regions. Nothing in Montagnier directs one of ordinary skill in the art to select SEQ ID NO:1 or SEQ ID NO:5 out of all of the potential conserved regions in the genome. The only guidance pointed to by the Examiner to lead one to the claimed sequences is the teaching of the present specification. This is clearly improper.

51. The above arguments have been considered and have not been found persuasive towards the withdrawal of the rejection.

52. It is noted with particularity that the claims at issue are highly similar to claims in related application 13/372,585, which were also rejected under 35 USC 103(a), where the rejection was predicated upon the same disclosure of Montagnier *et al.* It is noted that the Board of Patent Appeal & Interferences (Board), on 27 November 2012, affirmed the 103(a) rejection of all claims, which were likewise drawn to a pair of primers for amplification of conserved sequences found within the LTR region of HIV-1, and which had the same size as that claimed instantly.

53. Contrary to arguments of applicant, the Board held that the rejection was analogous to that of *KSR*. As stated at page 9 of the Board decision:

While Montagnier is arguably directed to the nef gene of HIV, that does not obviate Montagnier's teaching of the need for rapid tests for HIV, that the use of PCR is advantageous because it takes less than three days to complete, and the use of primer pairs from the conserved regions of the viral genome, such as the LTR region... Given the state of the art that the selection of appropriate primer pairs was known (see, e.g., Montagnier, col. 19, ll. 24-28), we agree with the Examiner that the selection of the primer pair recited in claim 14 would have been *prima facie* obvious to the ordinary artisan at the time of invention.

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Appellants' arguments that the three regions mentioned by Montagnier constitute over 50% of the virus genome do not convince us otherwise. The choice of any primer pair from the conserved regions of the HIV genome would have been *prima facie* obvious over the teachings of Montagnier. Again, we note that the sequence of the HIV genome was known, and the ordinary artisan would have been able to select appropriate primer pairs from the conserved regions of the HIV genome, as PCR was a known technique, as were the requirements for the selection of primer pairs to amplify a desired nucleic acid.

As in the present case, applicant/appellant, presented argument relating to an improper "obvious to try" rationale. The Board found such arguments non-persuasive. As set forth in the decision:

Appellants' arguments are again not found to be convincing. That is, we conclude that the Examiner has made the requisite fact findings to support an "obvious to try" rationale.

At page 24 of the response, argument is presented of unexpected results. This argument was also presented in the appeal brief in related application 13/372,585. There, the Board held:

To the extent that Appellants are arguing unexpected results, we note that the burden of demonstrating unexpected results rests on the party asserting them, and "it is not enough to show that results are obtained which differ from those obtained in the prior art; that difference must be shown to be an unexpected difference." *In re Klosak*, 455 F.2d 1077, 1080 (CCPA 1972). "Mere improvement in properties does not always suffice to show unexpected results." *In re Soni*, 54 F.3d 746, 751 (Fed. Cir. 1995). Moreover, it is well settled that results must be established by factual evidence. "Mere argument or conclusory statements in the specification does not suffice." *In re DeBlauwe*, 736 F.2d 699,705 (Fed. Cir. 1984).

Here, while Appellants point to Examples 4 and 5 of the Specification, it is unclear how those results demonstrate that the claimed primer pair has unexpected properties. First, the primer pair used in Examples 4 and 5 (SEQ ID 9/SEQ ID 5) is not the same as the claimed primer pair, and Appellants have provided no evidence on the record demonstrating that one would expect the same results for the claimed primer pair as obtained for the primer pair used in the Examples. Moreover, while Appellants assert that the gag primer pair is also highly conserved, the Specification only references a journal article for the gag primer pair (see Spec. pp. 17-18, Example 3). Appellants have provided no evidence to compare the conservation of the sequence of the claimed primer pair to the conservation of the gag primer pair used in Examples 4 and 5 to determine if the results were actually unexpected. As noted by the Federal Circuit, attorney argument cannot take the place of evidence lacking in the record. *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 595 (Fed. Cir. 1997).

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In view of the absence of direct evidence, and in view of the Board's decision, applicant's argument has not been found persuasive.

It is noted that applicant has not sought to appeal the decision of the Board in the '585 application and as such, the '585 application has gone abandoned. Such non-action by applicant is taken as tacit approval of, or agreement with, the decision of the Board.

54. For the above reasons, and in the absence of convincing evidence to the contrary, claims 36, 38, 41, 42, 46, 48, and 58-60 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of applicant's admissions.

Conclusion

55. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

56. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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57. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

58. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

59. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

Notice of References Cited	Application/Control No. 11/108,233		Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson		Art Unit 1634	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-4,772,547	09-1988	Heimer et al.	435/5
*	B	US-4,963,532	10-1990	Carter, William A.	514/44R
*	C	US-5,221,610	06-1993	Montagnier et al.	435/7.1
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.



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BIB DATA SHEET

CONFIRMATION NO. 5814

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
11/108,233	04/18/2005	435	1634	9310-22CT		
RULE						
APPLICANTS Jaap Goudsmit, Amsterdam, NETHERLANDS; Pieter Oudshoorn, Michielsgestel, NETHERLANDS; Suzanne Jurriaans, Monnickendam, NETHERLANDS; Vladimir Vladimirovich Lukashov, Dienen, NETHERLANDS;						
** CONTINUING DATA ***** This application is a CON of 09/463,352 01/21/2000 PAT 6,881,537 which is a 371 of PCT/EP98/04945 08/05/1998						
** FOREIGN APPLICATIONS ***** EUROPEAN PATENT OFFICE (EPO) 97202455.8 08/08/1997						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/18/2005						
Foreign Priority claimed	☒ Yes ☐ No	☐ Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
35 USC 119(a-d) conditions met	☒ Yes ☐ No	Initials	NETHERLANDS	1	25 14	16 5
Verified and Acknowledged	/BRADLEY L SISSON/ Examiner's Signature					
ADDRESS						
MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627 UNITED STATES						
TITLE						
NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1						
FILING FEE RECEIVED	FEES: Authority has been given in Paper			☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit		
2500	No. _____ to charge/credit DEPOSIT ACCOUNT					
	No. _____ for following:					

<i>Index of Claims</i> 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☒ T.D.		☐ R.1.47				
CLAIM		DATE								
Final	Original	10/04/2007	02/06/2008	06/22/2008	09/08/2008	02/23/2009	06/01/2009	09/09/2009	02/21/2010	01/17/2011
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<i>Index of Claims</i> 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L. Sisson	Art Unit 1634

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☒ T.D.		☐ R.1.47				
CLAIM		DATE								
Final	Original	10/04/2007	02/06/2008	06/22/2008	09/08/2008	02/23/2009	06/01/2009	09/09/2009	02/21/2010	01/17/2011
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	56	÷	N	N	N	N	N	N	N	N
	57					✓	✓	-	-	-

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL **(Submitted Only via EFS-Web)**

Application Number	11108233	Filing Date	2005-04-18	Docket Number (if applicable)	9310-22CT	Art Unit	1634
First Named Inventor	Jaap Goudsmit			Examiner Name	Bradley L. Sisson		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
 Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

☐ Other _____

☒ Enclosed

☒ Amendment/Reply

☐ Information Disclosure Statement (IDS)

☒ Affidavit(s)/ Declaration(s)

☒ Other

Certification and Request for Prioritized Examination under 37 CFR 1.102(e)

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
 (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(l) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to
 Deposit Account No 500220

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

Doc code: RCEX

Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (07-09)

Approved for use through 07/31/2012. OMB 0851-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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Signature of Registered U.S. Patent Practitioner			
Signature		Date (YYYY-MM-DD)	2013-06-03
Name	Robert A. Schwartzman, Ph.D.	Registration Number	50211

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

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Attorney Docket No. 9310-22CT
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.	Confirmation No. 5814
Application No.: 11/108,233	Group Art Unit: 1634
Filed: April 18, 2005	Examiner: Bradley L. Sisson
Title: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1	

June 3, 2013

Mail Stop Amendment
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

RESPONSE TO FEBRUARY 1, 2013 OFFICE ACTION

Sir:

This paper is responsive to the Office Action mailed February 1, 2013 regarding the above-referenced patent application and is being filed together with a Request for Continued Examination and a Request for Prioritized Examination. Please reconsider the rejections of the claims for at least the reasons presented in the following remarks.

If any extension of time for the accompanying response or submission is required, Applicants requests that this be considered a petition therefor. The Commissioner is hereby authorized to charge any additional fee, which may be required, or credit any refund, to our Deposit Account No. 50-0220.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 7 of this paper.

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-35. (canceled)

36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer ~~is a maximum of 50 nucleotides in length and~~ comprises (1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15 ~~10~~-26 nucleotides in length and comprising at least 15 ~~10~~ sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

~~(2) a promoter operably linked to said first oligonucleotide~~ being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

37-40. (canceled)

41. (currently amended) A primer set for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said set consisting of a first primer and a second primer,

wherein said first primer is ~~a maximum of 50 nucleotides in length and~~ comprises:
(1) a first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15 40-26 nucleotides in length and comprising at least 15 40 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; ~~and~~

(2) ~~a promoter operably linked to~~ said first hybridizing oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer comprises a second hybridizing oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

42-45. (canceled)

46. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer is ~~a maximum of 50 nucleotides in length and~~ comprises (1) a first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15 40-26 nucleotides in length, wherein said first

hybridizing oligonucleotide comprises at least 15 ~~40~~ sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) ~~a non-hybridizing promoter operably linked to said hybridizing oligonucleotide~~ being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer comprises a second hybridizing oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length, wherein said second hybridizing oligonucleotide comprises at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

47-49. (canceled)

50. (withdrawn) A test kit for the detection of HIV-1 nucleic acid in a sample comprising:

- a) the pair of oligonucleotide primers of any one of claims 36, 41, and 46; and
- b) one or more detectably labeled oligonucleotides comprising a nucleic acid sequence substantially complementary to at least part of the target sequence produced in an amplification reaction comprising the pair of oligonucleotide primers of (a).

51. (canceled)

52. (withdrawn) A method for the detection of HIV-1 nucleic acid in a sample, comprising:

a) contacting the sample with the pair of oligonucleotide primers of claim 36 under conditions whereby nucleic acid amplification can occur; and

b) detecting the presence of amplified HIV-1 nucleic acid, thereby detecting HIV-1 nucleic acid in the sample.

53. (withdrawn) A method for the detection of HIV-1 nucleic acid in a sample, comprising:

a) contacting the sample with the primer set of claim 41 under conditions whereby nucleic acid amplification can occur; and

b) detecting the presence of amplified HIV-1 nucleic acid, thereby detecting HIV-1 nucleic acid in the sample.

54. (canceled)

55. (withdrawn) A method for the detection of HIV-1 nucleic acid in a sample, comprising:

a) contacting the sample with the pair of oligonucleotide primers of claim 46 under conditions whereby nucleic acid amplification can occur; and

b) detecting the presence of amplified HIV-1 nucleic acid, thereby detecting HIV-1 nucleic acid in the sample.

56. (withdrawn) A method for amplifying HIV-1 nucleic acid in a sample, comprising contacting the sample with the pair of oligonucleotide primers of any one of claims 36, 41, and 46 under conditions whereby an amplification reaction can occur.

57. (canceled)

58. (currently amended) The pair of oligonucleotide primers of claim 36, wherein said first oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26

~~nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:~~

~~SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and~~

said second oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

59. (currently amended) The primer set of claim 41, wherein ~~said first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:~~

~~SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and~~

said second hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

60. (currently amended) The pair of oligonucleotide primers of claim 46, wherein ~~said first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:~~

~~SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and~~

said second hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

61. (canceled)

REMARKS

Upon entry of the foregoing amendment, claims 36, 41, 46, 50, 52, 53, 55, 56, and 58-60 are pending in the application, with 36, 41, and 46 being the independent claims. Claims 50, 52, 53, 55, and 56 have been withdrawn by the Examiner as being directed to a non-elected invention. Claims 38, 42, and 48 have been canceled without prejudice or disclaimer. Claims 36, 41, 46, and 58-60 have been amended to claim the invention with more particularity. Support for the amendments is found in the claims as originally filed. No new matter has been added.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections Under 35 U.S.C. § 112

Claims 36, 38, 41, 42, 46, 48, and 58-60 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. (Office Action, page 3). Applicants respectfully traverse this rejection.

The Examiner states that HIV-1 comprises two LTR regions and that the claimed primers are not limited as to their hybridizing to regions found in one or the other or both LTRs. (Office Action, page 5). The Examiner further states that the concept of a first primer containing a first oligonucleotide and a promoter sequence and having a maximum length of 50 nucleotides is not found in the disclosure and is deemed to constitute new matter. (Office Action, page 6). The Examiner also states that the disclosure does not provide a description of any promoter that can be combined with a first oligonucleotide of 26 nucleotides in length and not exceed the upper limit of 50 nucleotides for the complete length of the first primer. (Office Action, page 6).

Applicants respectfully disagree. Claims 38, 42, and 48 have been canceled, rendering that portion of the rejection moot. Applicants point out that the two LTRs in the genome of HIV-1 are identical to each other. The LTR sequences to which the presently claimed oligonucleotides are fully complementary are present in both the 5' and 3' LTRs. Thus, the primer sets are capable of amplifying a portion of the LTR in both the 5' and 3' LTRs.

As amended, the claims do not recite that the first primer has a maximum length of 50 nucleotides. Thus, the new matter issue has been rendered moot.

As amended, the claims are directed in part to a first oligonucleotide operably linked to a T3, T7, or SP6 promoter. These promoters are well known in the art and are adequately described in the specification (page 6, lines 2-4). Thus, it is clear that Applicants were in possession of the claimed invention as of the effective filing date of the present application.

Applicants respectfully request that the rejection of claims 36, 38, 41, 42, 46, 48, and 58-60 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 36, 38, 41, 42, 46, 48, and 58-60 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Montagnier *et al.* (U.S. Patent No. 5,221,610, hereafter “Montagnier”) in view of Applicants’ alleged admissions. (Office Action, page 7). Applicants respectfully traverse this rejection.

The Examiner alleges that Applicants have made an admission in the specification that the env gene of HIV has higher sequence variation between subtypes than other regions. (Office Action, pages 10-11). The Examiner alleges that Applicants have made an admission that various techniques for amplifying nucleic acid are known in the art. (Office Action, page 11). The Examiner quotes Montagnier regarding “primer pairs and probes derived from highly conserved regions of the viral genome, such as the LTR, qao [sic, gag], and env regions of HIV-1” and asserts that one would have been amply motivated and would have also had a most reasonable expectation of success in identifying primers from the LTR region from the finite number of possible sequences. (Office Action, pages 11-12).

Applicants respectfully disagree. Claims 38, 42, and 48 have been canceled, rendering that portion of the rejection moot.

The United States Supreme Court has articulated that obviousness under § 103(a) is determined by an analysis of the following factors: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The obviousness or nonobviousness of the subject

matter is to be determined based on these considerations, however, secondary considerations such as commercial success, long-felt but unresolved needs and the failure of others can be utilized to determine the circumstances surrounding the origin of the invention. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1730 (2007). If such secondary considerations exist, they must be considered. *See Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538-1539 (Fed. Cir. 1983).

In *KSR*, the Supreme Court also made clear that predictable variations are likely obvious, but unpredictable variations are not:

If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative - a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

KSR at 1740.

The Court also recognized that when the prior art taught away from the claimed invention, the invention was more likely to be non-obvious: "when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR* at 1740 (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1996)).

The Court also emphasized the importance of identifying "a reason" that a person of ordinary skill in the relevant field would have combined the elements in the fashion claimed by the new invention. *Id.* at 1731. The Court also emphasized that this analysis should be made explicit:

Often it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit.

Id. at 1740-1741 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

Claim 36 is representative of the present invention.

36. A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer comprises a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15-26 nucleotides in length and comprising at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA;

said first oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

Applicants assert that Montagnier does not explicitly point to the development of primer pairs targeted to the LTR. The sentence that the Examiner quotes from Montagnier must be considered for all it teaches, not just the portion of the sentence highlighted by the Examiner. The cited sentence in full states that “[f]or this reason, the PCR technique is preferably carried out with several primer pairs and probes derived from highly conserved regions of the viral genome, such as the LTR, qao [sic, gag], and env regions of HIV-1.” (column 19, line 67 to column 20, line 2). Thus, Montagnier does not specifically point to the LTR as the Examiner

asserts, it directs one to use any highly conserved region of the viral genome, and provides the LTR, gag, and env regions as examples. The sentence in Montagnier, which is the only mention in the patent of primers directed to conserved regions, would be interpreted by one of ordinary skill in the art to impart two teachings: (1) that any highly conserved region anywhere in the HIV-1 genome is likely to be effective; and (2) that highly conserved regions may be found in the LTR, gag, and env regions, which make up more than 50% of the genome of HIV-1. Because Montagnier points to regions making up more than half of the genome and does not single out the LTR over the other listed regions or any other highly conserved region, the Examiner overstates the relevancy of the teaching of Montagnier when the Examiner asserts that Montagnier provides "explicit guidance to identify primers in this very region." (Office Action, page 12).

In response to Applicants' arguments that Montagnier points to conserved regions throughout the HIV genome, the Examiner states that the env gene was known in the art to be the most variable of all the genes, implying that the LTR is more conserved and that one of ordinary skill in the art would have been motivated to choose that part of the HIV genome that is not subject to such high variability. (Office Action, page 12).

Applicants respectfully disagree. The Examiner's reasoning regarding the variability of the env gene and the selection of primer pairs is flawed. Even if the env gene is the region of the HIV-1 genome with the highest variability, one of ordinary skill in the art was aware that the env gene contained conserved sequences. This is apparent from the references disclosed in the present specification and discussed by the Examiner. In the sentences regarding env gene variability in the specification that are quoted by the Examiner (starting at page 2, line 13), the specification refers to a study by McCutchan *et al.* (*J. AIDS* 4:1241(1991)) in which "primers were chosen from relatively conserved regions in gag, env and LTR" (page 2, lines 18-20). In the paragraph quoted by the Examiner beginning on page 2, line 33, the specification cites another study (Engelbrecht *et al.*, *J. Virol. Meth.* 55:391 (1995)) on the development of an assay "using env, gag and LTR primer pairs to detect subtypes in the Western Cape, South Africa." These cited references provide evidence that one of ordinary skill in the art was aware of conserved sequences within the env gene and actively sought to develop primer pairs directed to those conserved sequences as well as conserved sequences throughout the genome. Thus, the

Examiner's conclusion that one would have been motivated to specifically choose the LTR region is incorrect.

The Examiner acknowledges that Montagnier does not teach primers having the claimed sequences SEQ ID NO:1 or SEQ ID NO:5 but states that Applicants teach in the specification how these sequences are highly conserved in HIV. (Office Action, page 12). The Examiner is of the opinion that it would have been obvious to select these sequences as well as the claimed oligonucleotide length based on the explicit guidance by Montagnier to select just such highly conserved sequences. (Office Action, pages 12-13).

Applicants respectfully disagree. As stated above, the single sentence in Montagnier regarding primer pairs directed to highly conserved regions suggests at most that any highly conserved region in the genome will be sufficient to detect HIV-1 variants. As the Examiner acknowledges, Montagnier does not disclose primers comprising SEQ ID NO:1 or SEQ ID NO:5. The Examiner's conclusion that it would have been obvious to select primers comprising SEQ ID NO:1 or SEQ ID NO:5 because the present specification teaches that these sequences are highly conserved in HIV is an example of hindsight reasoning by the Examiner. The Examiner's reasoning appears to be that Montagnier suggests using any conserved HIV sequence, the specification discloses such a sequence, so one of ordinary skill in the art would have picked the disclosed sequence. This reasoning is improper for an obviousness analysis. The genome of HIV-1 is replete with highly conserved regions as acknowledged by Montagnier, which points to the LTR, gag, and env regions as examples of sections of the HIV-1 genome that contain such conserved regions. Nothing in Montagnier directs one of ordinary skill in the art to select SEQ ID NO:1 or SEQ ID NO:5 out of all of the potential conserved regions in the genome, much less to pair them together. The only guidance pointed to by the Examiner to lead one to the claimed sequences is the teaching of the present specification. This is clearly improper.

The Examiner states that the present claims are directed to a composition of primers, not a method, and the claims do not prohibit the combining of the resultant primer pairs with other primer pairs in a multiplex reaction. (Office Action, page 13). The Examiner therefore concludes that the fact that Montagnier teaches combining primers to detect variants of HIV-1

because a single primer pair may not produce reliable results does not overcome the alleged obviousness of the claimed primer sets.

Applicants respectfully disagree. Montagnier teaches that any single primer pair may not produce reliable results due to genetic variations or deletions in the regions targeted for amplification and therefore teaches that it is preferred to carry out amplification with several primer pairs (column 19, line 60 to column 20, line 2). Thus, one of ordinary skill in the art reading Montagnier would understand that no single primer pair would detect most or all variants of HIV-1. In contrast, the presently claimed primer pairs are capable of detecting all HIV-1 variants tested in the disclosed examples. Thus, the presently claimed invention provides superior results that obviate the need for multiple primer pairs as taught by Montagnier. As Montagnier provides no teaching or suggestion that primer pairs having this ability are possible, it cannot render the present claims obvious. While the Examiner suggests that the claimed primer pairs can be combined with other primer pairs for use in a multiplex amplification reaction, the fact is that the claimed primer pairs have superior properties that overcome the need for a multiplex amplification, a fact that could not have been predicted by one of ordinary skill in the art based on a reading of Montagnier. For at least this reason, the claimed invention is non-obvious.

The Examiner further alleges that Applicants admit that promoter-primers are known in the art. (Office Action, pages 13-14). The Examiner is of the opinion that one of ordinary skill in the art would have been motivated to include promoters on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences. (Office Action, page 14).

Applicants respectfully disagree. The claimed primer pair sequences are non-obvious for at least the reasons discussed above. Any alleged knowledge of the use of promoter-primers would not render the claimed invention obvious as the primer pairs themselves remain non-obvious.

The Examiner states that the LTR is less than 1 kb in size and that, given such a small target area, and specific guidance as to where and what to be looking for, there exists but a finite number of identified, predictable solutions as there exists but a finite number of highly conserved regions with the LTR of HIV. (Office Action, pages 15-16).

Applicants respectfully disagree. As stated above, Montagnier does not direct one of ordinary skill in the art to the LTR region specifically, it directs one to any highly conserved region in the HIV-1 genome. At a minimum, this includes the LTR, gag, and env regions of the genome as stated by Montagnier. The LTR has a length of about 640 base pairs, while the gag and env genes have a length of about 1500 and 2570 base pairs, respectively. These three regions (including both LTRs) add up to a total of about 5330 base pairs, more than 50% of the total HIV-1 genome. Even if one were to limit a search to the LTR, gag, and env regions based on the disclosure of Montagnier, more than half the genome would still have to be searched for highly conserved sequences. Thus, one of ordinary skill in the art has not been “[g]iven such a small target area” as suggested by the Examiner. Furthermore, Montagnier does not provide any “specific guidance as to where and what to be looking for” as suggested by the Examiner. Montagnier provides no specific guidance at all in the one sentence disclosure regarding conserved sequences. In particular, Montagnier provides absolutely no guidance on what to look for, *e.g.*, no definition of “highly conserved.” Furthermore the Examiner fails to support his statement that “there exists but a finite number of ‘highly conserved’ regions with the LTR of HIV” with any evidence other than the total length of the LTR. Given the large target area disclosed in Montagnier and the total lack of guidance as to what to look for, there clearly is more than a finite number of identified, predictable solutions. For at least this reason, the claimed invention is non-obvious.

The Examiner alleges that the present claims are highly similar to claims in related Application No. 13/372,585, which were rejected as obvious over the same disclosure of Montagnier, along with other cited references. This rejection was affirmed by the Board of Patent Appeals and Interferences (BPAI). (Office Action, page 17). The Examiner quotes the BPAI decision as stating that the choice of any primer pair from the conserved regions of the HIV genome would have been *prima facie* obvious over the teachings of Montagnier. (Office Action, page 18). The Examiner notes that Application No. 13/372,585 has not been appealed and has gone abandoned, which the Examiner takes as tacit approval of, or agreement with, the decision of the BPAI. (Office Action, page 19).

Applicants respectfully disagree that a *prima facie* case of obviousness has been made for at least the reasons recited above. Applicants also note that the Examiner’s indication that the

abandonment of Application No. 13/372,585 is tacit agreement with the BPAI decision is an unfounded and inappropriate assumption. There are any number of reasons to allow an application to go abandoned, including filing of a continuation application, budgetary concerns, or a change in prosecution strategy. Applicants assert that they do not agree with the decision of the BPAI.

However, Applicants provide herewith evidence of unexpected superior results for the primer pairs of the claimed invention that overcomes any alleged *prima facie* case of obviousness. Applicants submit concurrently herewith a Declaration of Ali Laayoun, Ph.D. Pursuant to 37 C.F.R. § 1.132 (hereinafter, "the Laayoun Declaration"). The Laayoun Declaration supports Applicant's assertions regarding the non-obviousness of the claimed primer pairs by demonstrating the superiority of the claimed primer pairs in terms of amplification efficiency and detection sensitivity in nucleic acid amplification assays compared to other primers targeting the HIV LTR.

The Laayoun Declaration describes studies that were carried out in a laboratory at bioMérieux (the assignee of the present application) to perform a direct comparison of the primer pairs of the present invention with the P3 and P4 primers of Bell & Ratner (*Aids Res Human Retroviruses* 5:87-95 (1989)), a previous publication disclosing primers targeted to the HIV-1 LTR (cited in the Information Disclosure Statement filed July 25, 2005). Both the primer pairs of the present invention and the primer pair of Bell & Ratner are fully complementary to the sequence of HIV-1 strain HXB2, the template used in the described experiments. Paragraphs 5-11 of the Laayoun Declaration describe the results of a first series of amplification assays (nucleic acid sequence-based amplification (NASBA), polymerase chain reaction (PCR), and reverse transcription-polymerase chain reaction (RT-PCR)) comparing the performance of a primer pair of the claimed invention (SEQ ID NOs: 1 and 5) with the P3 and P4 primers of Bell & Ratner.

The NASBA results are described in paragraph 8 and Figures 2-6. Each primer pair was tested in a NASBA assay starting with different amounts of HIV template ranging from 10^5 to 10^1 target copies. The claimed primer pair was highly effective at all template ranges, providing a short time to positivity, a clear plateau, and a steep slope, all indications of a highly efficient primer pair. In contrast, the P3 and P4 primers could not detect template at a level less than 10^4

target copies (see Fig. 4). Even at higher levels of template, the P3 and P4 primers exhibited a longer time to positivity and a lower plateau value, and did not achieve a steep slope, indicating a less efficient primer pair (see Figs. 2 and 3).

The PCR results are described in paragraph 9 and Figures 7-11. Each primer pair was tested in a PCR assay starting with different amounts of HIV template ranging from 2×10^5 to 2×10^1 target copies. The claimed primer pair was effective at all template ranges. In contrast, the P3 and P4 primers could not detect template at a level less than 2×10^4 target copies (see Fig. 9). Even at a template level of 2×10^4 , the P3 and P4 primers did not produce the signal strength produced by the primer pair of the claimed invention (see Fig. 8).

The RT-PCR results are described in paragraph 10 and Fig. 12. The claimed primer pair produced a stronger signal than the P3 and P4 primers (see Fig. 12).

Paragraph 12 summarizes the results for the first series of amplification assays indicating that the claimed primer pair is about 1000-fold more sensitive than the LTR primer pair of Bell & Ratner. The results indicate not all primer pairs derived from the HIV genome or even those derived only from the LTR have the same sensitivity in amplification assays. The primer pairs of the presently claimed invention provide a clear advantage over other primer pairs derived from the LTR as exemplified by the primer pair of Bell & Ratner. This result is unexpected and overcomes the *prima facie* assumption that any primer pair targeted to the HIV genome would be obvious.

The Laayoun Declaration also describes the results of a second series of NASBA amplification assays in paragraphs 12-13 and Figs. 13-21. In this series of experiments a series of variants of the primers of SEQ ID NOs: 1 and 5 that are encompassed by the present claims were tested for activity. The variants include primers comprising 10 nucleotides from the 5' or 3' end of SEQ ID NO: 5 extended an additional 8, 10 or 12 nucleotides (primers 5A-5F) and extensions of SEQ ID NO: 1 by 8 nucleotides on the 3' or 5' end (primers 1B-1C) (see Fig. 13). Every combination of upstream primer (including P4) and downstream primer (including P3) was tested in the NASBA assay with different amounts of HIV template ranging from 2×10^5 to 2×10^1 international units (IU)/reaction. The results are shown in Figs. 14-21.

In each of Figs. 14-20 it can be seen that the upstream primers SEQ ID NO: 5 and variants 5A-5F were capable of creating an effective primer pair when paired with the

downstream primers SEQ ID NO:1 (labeled 1A in the figures), 1B, and 1C, although not all pairs are equally efficient. In contrast, the upstream primers were mostly ineffective when paired with the downstream primer P3. Only SEQ ID NO: 5 and 5F were capable of limited detection of HIV-1 when paired with P3 and only at the highest template concentration (see Figs. 14 and 20). Even the less efficient pairs of variants of the claimed invention were more effective than any single variant matched up with P3.

Similarly, when upstream primer P4 was paired with 1A, 1B, or 1C, the pair was at best only slightly effective (see Fig. 21). The P4/1B primer pair was the only pair capable of even limited detection of HIV-1 and this was only at the highest template concentration (see Fig. 21).

Paragraph 14 summarizes the results for the second series of amplification assays indicating that the claimed primer pairs provide unexpectedly superior results than that provided by the primer pair of Bell & Ratner. The primer pairs of the present invention are consistently more sensitive than those of Bell & Ratner, detecting levels of HIV-1 as low as 10^1 IU/reaction (Fig. 16) and consistently as low as 10^2 IU/reaction (see Figs. 14-20), while the primer pair of Bell & Ratner was unable to detect HIV-1 even at levels of 10^3 IU/reaction (Fig. 21).

The results show that the all of the variant primer pairs encompassed by the present claims that were tested exhibited superior results. In each case, the upstream primers of the present invention having extensions of 8, 10 and 12 nucleotides at the 5' or the 3' end of SEQ ID NO:5 (primers 5A through 5F) showed greater sensitivity and thus better ability to detect HIV-1 than the P4 primer of Bell & Ratner when combined with the P3 primer of Bell & Ratner (Fig. 21) or a downstream primer of the present invention (primers 1A-1C; Figs. 14-20). Similarly, the downstream primers of the present invention having extensions of 8 nucleotides at the 3' or the 5' end of SEQ ID NO:1 (primers 1B and 1C) showed greater sensitivity and thus better ability to detect HIV-1 than the P3 primer of Bell & Ratner when combined with the P4 primer of Bell & Ratner (Fig. 21) or an upstream primer of the present invention (SEQ ID NO:5 and 5A-5F; Figs. 14-20).

Even those primer pair combinations of the present invention that do not perform as well as other primer pair combinations of the invention still perform better than the Bell & Ratner primer pair. In each case, under the same conditions, the time to positivity as well as the slope of amplification is better for the primer pairs of the present invention than that observed for the

primer pair of Bell & Ratner (Figs.14-21). Further, the above experiments show that the primer pairs of the present invention perform better than a pair of primers in which one of the primers is a Bell & Ratner primer and the other is a primer of the present invention (P3 in Figs 14-20 and P4 in Fig. 21).

These results demonstrate that the primer pairs of the present invention are unexpectedly superior to other primer pairs derived from the LTR of HIV-1 in terms of amplification efficiency and detection sensitivity of HIV-1. Further, the unexpected superiority is seen across the genus of primers encompassed within the scope of the present claims. This superiority is surprising in part because the primers of the present invention and the primers of Bell & Ratner are all fully complementary to the sequence of HIV-1 strain HXB2, the template used in the experiments. The significant superiority of the claimed primers over the closest prior art as demonstrated in a direct comparison is more than sufficient to outweigh any alleged *prima facie* case of obviousness. Accordingly, Applicants respectfully submit that the claimed primers were not obvious as of the effective filing date of the present application.

Applicants respectfully request that the rejection of claims 36, 38, 41, 42, 46, 48, and 58-60 under 35 U.S.C. § 103(a) be withdrawn.

Rejoinder of claims

Applicants further specifically request that claims 50, 52, 53, 55, and 56 be rejoined and examined in the present application, once a determination is made that the composition claims under examination are allowable. Specifically, if the composition claims 36, 41, 46, and 58-60 are found to be allowable, applicants request that the Examiner review and examine claims 50, 52, 53, 55, and 56, which depend from these composition claims, according to the practice of rejoinder as set forth in section 821.04 of the MPEP. In particular, it is stated therein that if a product claim is elected in a restriction and then found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim are to be rejoined.

CONCLUSION

Accordingly, Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any small matters outstanding of resolution, he is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

No fee other than those accompanying this response is believed to be due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



Robert A. Schwartzman, Ph.D.
Registration No. 50,211

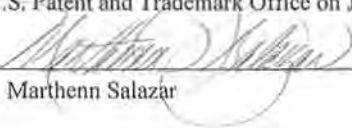
Customer Number 20792

Myers Bigel Sibley & Sajovec, P.A.
P.O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on June 3, 2013.

Signature: _____


Marthenn Salazar

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.

Application No.: 11/108,233

Filed: April 18, 2005

Title: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1

Confirmation No. 5814

Group Art Unit: 1634

Examiner: Bradley L. Sisson

Mail Stop Amendment

Commissioner for Patents

PO Box 1450

Alexandria, VA 22313-1450

**Declaration of Ali Laayoun, Ph.D.
Pursuant to 37 C.F.R. § 1.132**

I, **Ali Laayoun**, do hereby declare and say as follows:

1. I am the Director of Chemical Research & Analytical Technologies, R&D, Molecular Biology, bioMérieux, sa, Centre Christophe Mérieux, 5 rue des berges, 38024- Grenoble, which is the assignee of US Application No. 11/108,233 (the '233 application) and of the subject matter claimed therein.

2. I received a Ph.D. in Bio-Organic Chemistry at the Université J. Fourier de Grenoble, France in 1992 and a Master's Degree in Organic & Physical Chemistry at the Université J. Fourier de Grenoble, France in 1989. From October 1992 to July 1994, I was a postdoctoral researcher at City of Hope National Medical Center, Department of Cell & Tumor Biology (Duarte, California) where I conducted a research project on human DNA methylation; and from September 1994 to March 1995, I was an assistant professor at the University of Geneva, Switzerland. In February 1995, I became the nucleic acids laboratory manager at bioMérieux where I worked in the area of nucleic acid chemistry and oligonucleotides/probes development and management. This work included collaborations with academic labs and private companies. In 2000, I became a group leader at bioMérieux in the development of new and innovative approaches for nucleic acid detection on chips and in homogeneous format for *in vitro* diagnostic applications, and in 2003, I took on my present position of Director of Molecular Technologies and then Chemical Research & Analytical Technologies at bioMérieux. I have authored and co-authored over 30 publications in the area of nucleic acid chemistry and nucleic acid detection. A *curriculum vitae* is attached herewith at Tab A.

3. The studies described below were carried out in a laboratory at bioMérieux. These studies demonstrate that the primers of the present invention have superior kinetics when compared with other exemplary primers taken from the long terminal repeat (LTR) region of the HIV-1 virus.

4. A series of amplification assays were performed, including polymerase chain reaction (PCR), nucleic acid sequence-based amplification (NASBA) and reverse transcription-polymerase chain Reaction (RT-PCR), with various primer pairs comparing the performance of primers of the claimed invention (SEQ ID NOs:1 and 5) with the P3 and P4 primers of Bell & Ratner (*Aids Res Human*

Retroviruses 5:87-95 (1989)), a previous publication disclosing primers targeted to the HIV-1 LTR. The nucleotide sequence for each primer pair is derived from the LTR of the HIV-1 virus.

5. First series of assays

The nucleotide sequences of the primer pairs used in this set of assays are set forth below along with a diagram showing their position in the LTR of HIV-1 virus HXB2.

NASBA PRIMERS

Primer	Sequence
SEQ ID NO:1 (with promoter)	5' aattctaatacgactcactatagggaga GGG CGC CAC TGC TAG AGA
SEQ ID NO:5	5' CTC AAT AAA GCT TGC CTT GA
P4 Bell & Ratner	5' TCA ATA AAG CTT GCC TTG AGT GCT TCA AGT
P3 Bell & Ratner (with promoter)	5' aattctaatacgactcactatagggaga GTC CCT GTT CGG GCG CCA CT

PCR PRIMERS

Primer	Sequence
SEQ ID NO:1	5' GGG CGC CAC TGC TAG AGA
SEQ ID NO:5	5' CTC AAT AAA GCT TGC CTT GA
P4 Bell & Ratner	5' TCA ATA AAG CTT GCC TTG AGT GCT TCA AGT
P3 Bell & Ratner	5' GTC CCT GTT CGG GCG CCA CT

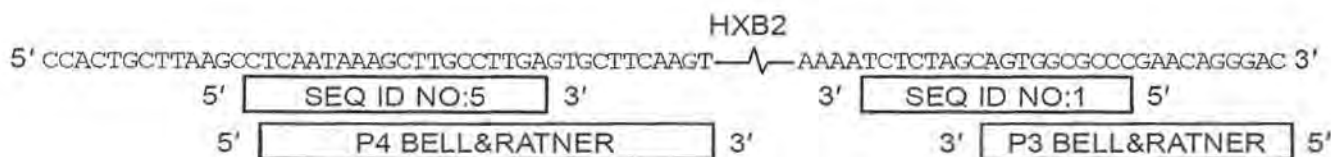


FIG. 1

6. The reaction conditions for the three different amplification techniques tested were as follows:

A. NASBA

- 70 mM KCl
- 0.2 μ M of each primer
- 0.1 μ M of LTR-Molecular Beacon
- 12 mM $MgCl_2$
- 2 mM rNTPs
- 1 mM dNTPs
- 0.5 mM rITP

15% DMSO
32 units T7 RNA Polymerase
Trehalose
0.08 units RNaseH
6.4 units AMV-RT
5 mM DTT

B. PCR

50 mM KCl
125 nM of each primer
50 nM Taqman Probe
1.5 mM MgCl₂
0.2 mM dNTPs
0.75 units Taq Polymerase

C. RT-PCR

Titan One Tube RT-PCR kit (Roche) with:
0.1 mM of each primer
40 nM Taq man Probe
1.5 mM MgCl₂
5 mM DTT

D. Template material:

- i. DNA (PCR): Recombinant DNA Clone; vector pG30 with a LTR insert (775nt, HXB2)
- ii. RNA (NASBA and RT-PCR): Working reference solution; produced from viral lysate with HIV1 virus HXB2 nucleotide sequence.

7. Figures 2-12 (in sections 8-10, below) show the results of the above amplification reactions. The figures differ by the type of assay: NASBA (Figures 2-6), PCR (Figures 7-10), RT-PCR (Figure 11) and the amount of template that the assay started with (NASBA, 10^5 - 10^1 target copies; PCR 2×10^5 - 2×10^1 target copies). Additionally, the primer pairs were tested in the presence of No Template (NT). In Figures 2-11, the units for the Y-axis are "fluorescence units."

In each of the graphs below 1+5 represents SEQ ID NOs:1 and 5; P3+P4 represents the primer pair of Bell & Ratner, 1+5 NT represents SEQ ID NOs:1 and 5 without template present, and P3+P4 NT represents the primer pair of Bell & Ratner without template present.

8. NASBA Results

In a NASBA assay, three parameters are relevant: (1) time to positivity, (2) plateau value and (3) slope of the amplification curve.

(1) "Time to positivity" is the time that it takes the enzymes in a NASBA reaction to generate sufficient amplicons for the fluorescent probe to hybridize to and generate a signal, the signal being

significantly higher as compared with the negative “no template” (NT) reaction. In these experiments, the probe is a molecular beacon (MB).

(2) “Plateau value” is reached when the amplicons are being formed in excess, while the amount of probe present is limited. Therefore, achieving a plateau value shows that a large amount of amplicon is being formed. A curve in which the probe signal does not reach a plateau indicates that the amount of amplicon generated is not sufficient to hybridize and light up all of the probes present in the reaction. The plateau of each curve should roughly reach the same level of fluorescent signal in reactions in which equal amounts of probe are being used. This level of signal is expected to be reached since in any high quality amplification reaction an excess of amplicons should be generated as compared to the amount of probe present. This provides each probe in the reaction mixture the opportunity to hybridize to an amplicon and produce a signal. Thus, a lower plateau value observed under otherwise equivalent conditions indicates that the amount of amplicon formed is less as compared with a reaction mixture that reaches a higher plateau value.

(3) A steep slope of an amplification curve indicates good amplification efficiency and is a measure of the quality of a primer pair. Primer pairs should be compared at the same concentration. Thus, curves showing the steepest slope are indicative of the efficiency of the primer pair in the amplification reaction.

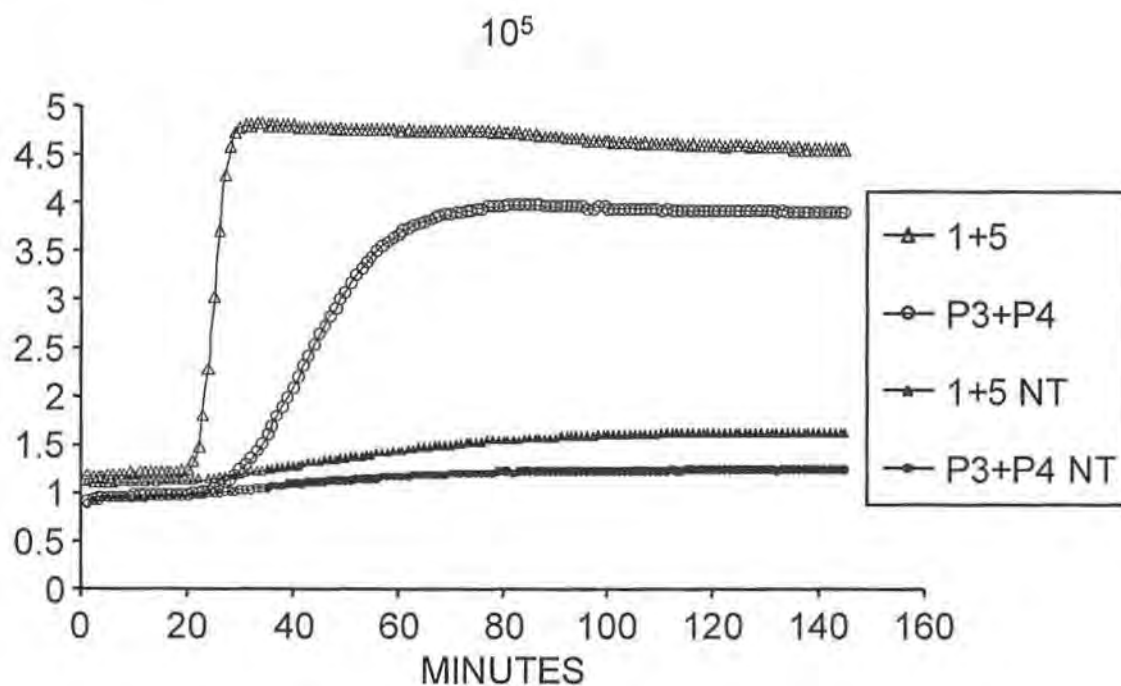


FIG. 2

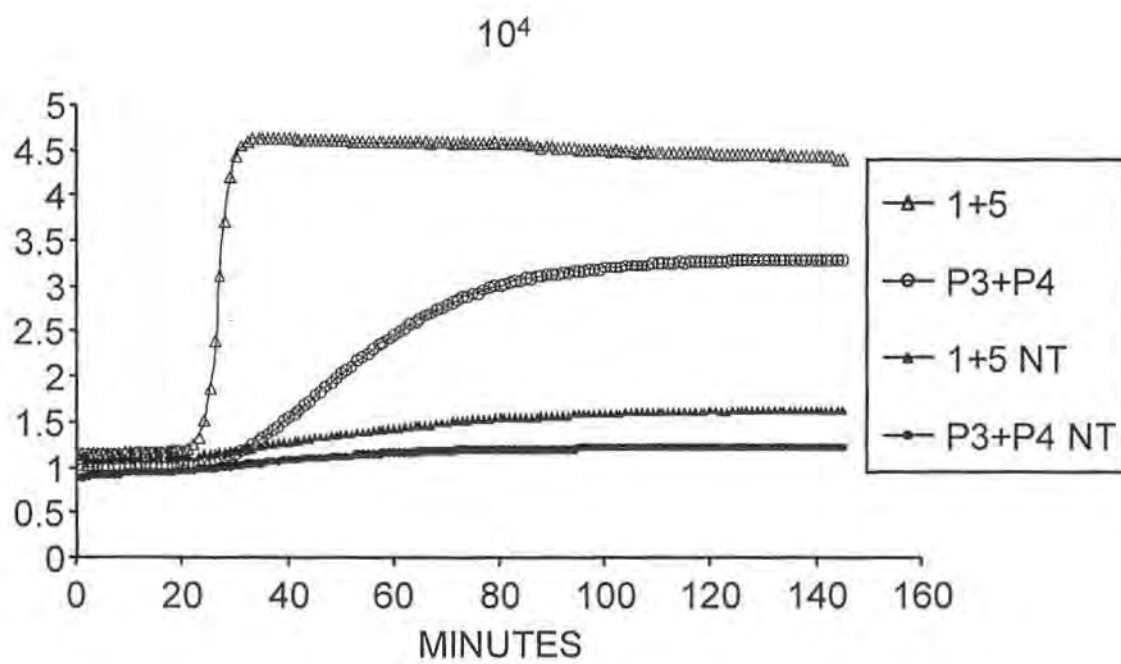


FIG. 3

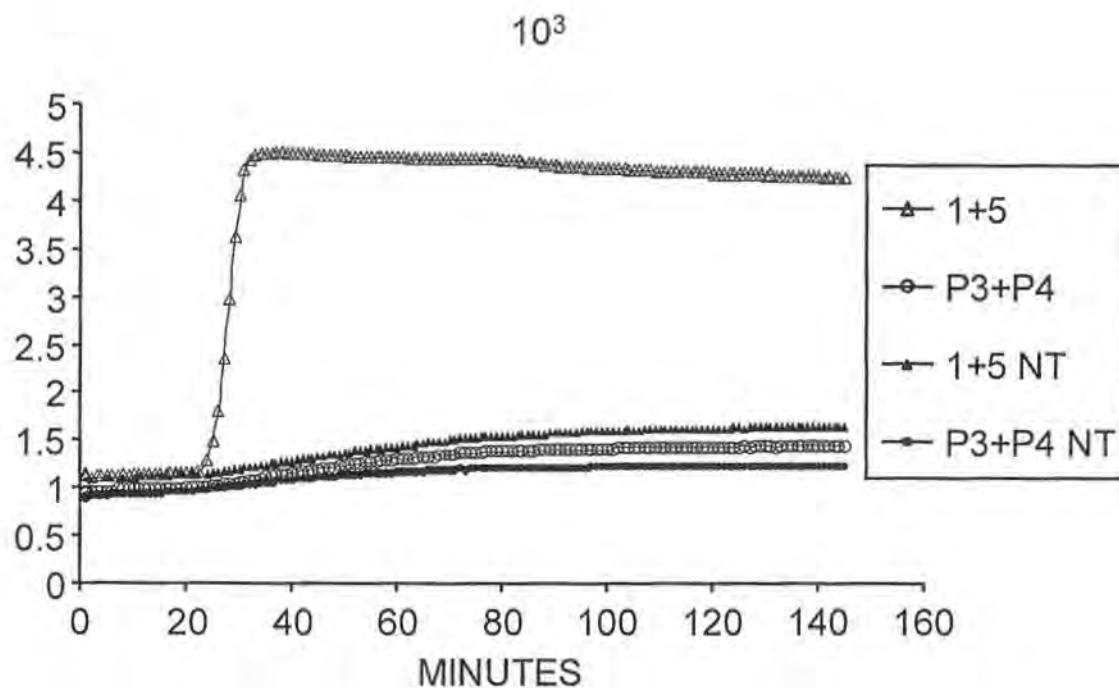


FIG. 4

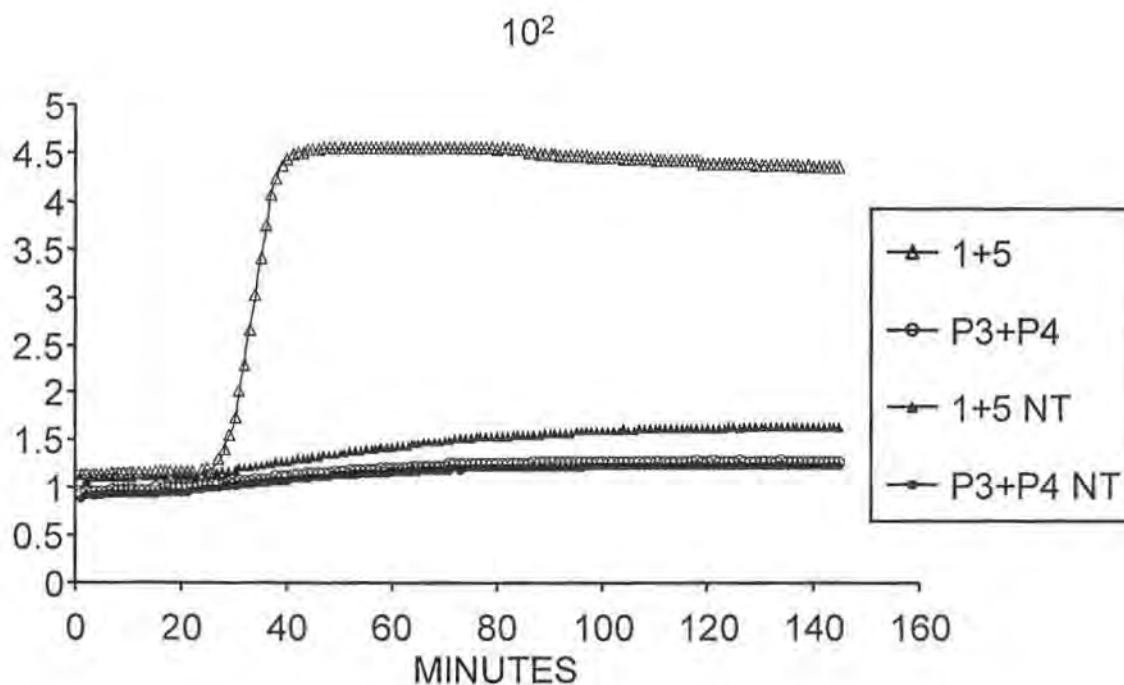


FIG. 5

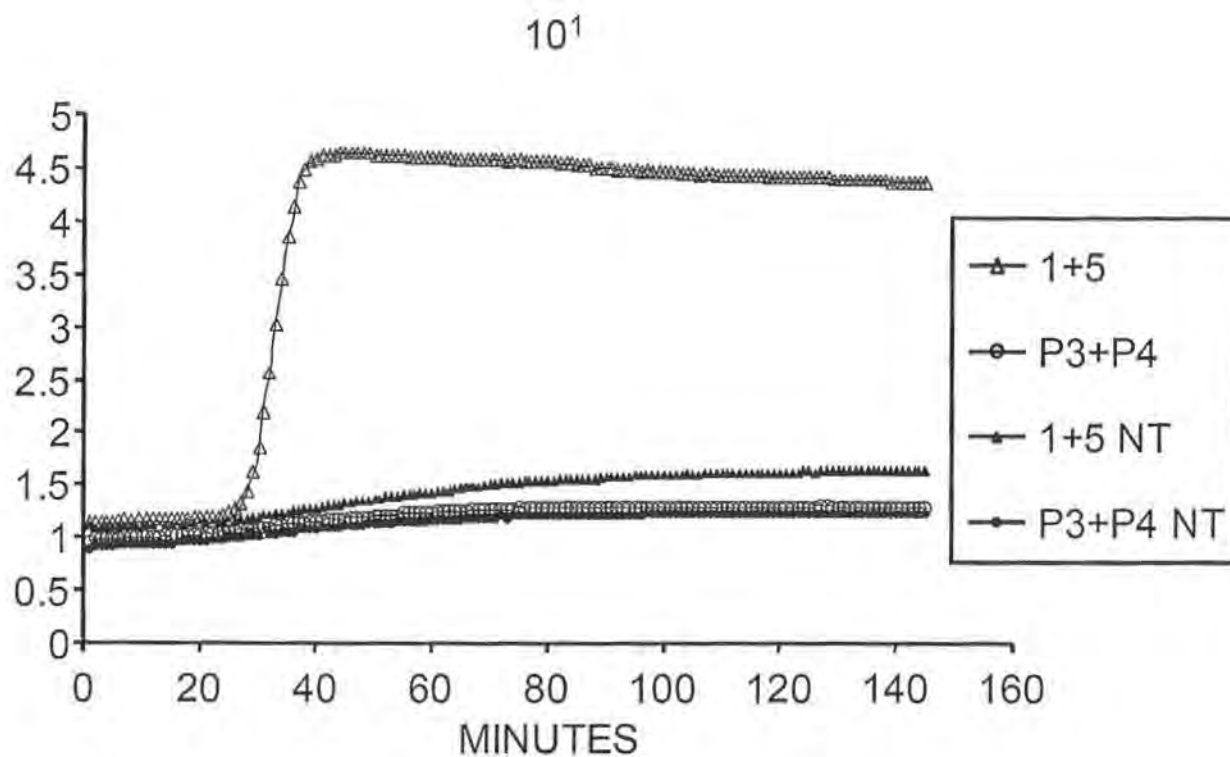


FIG. 6

9. PCR Results

The “time to positivity” (TTP) factor for the NASBA reaction is comparable to the “Ct” value in a PCR assay. The Ct value is defined as the PCR cycle at which the probe (Taqman probe) generates a signal above the background signal. A low Ct value is an indication of a very efficient amplification and a good primer pair.

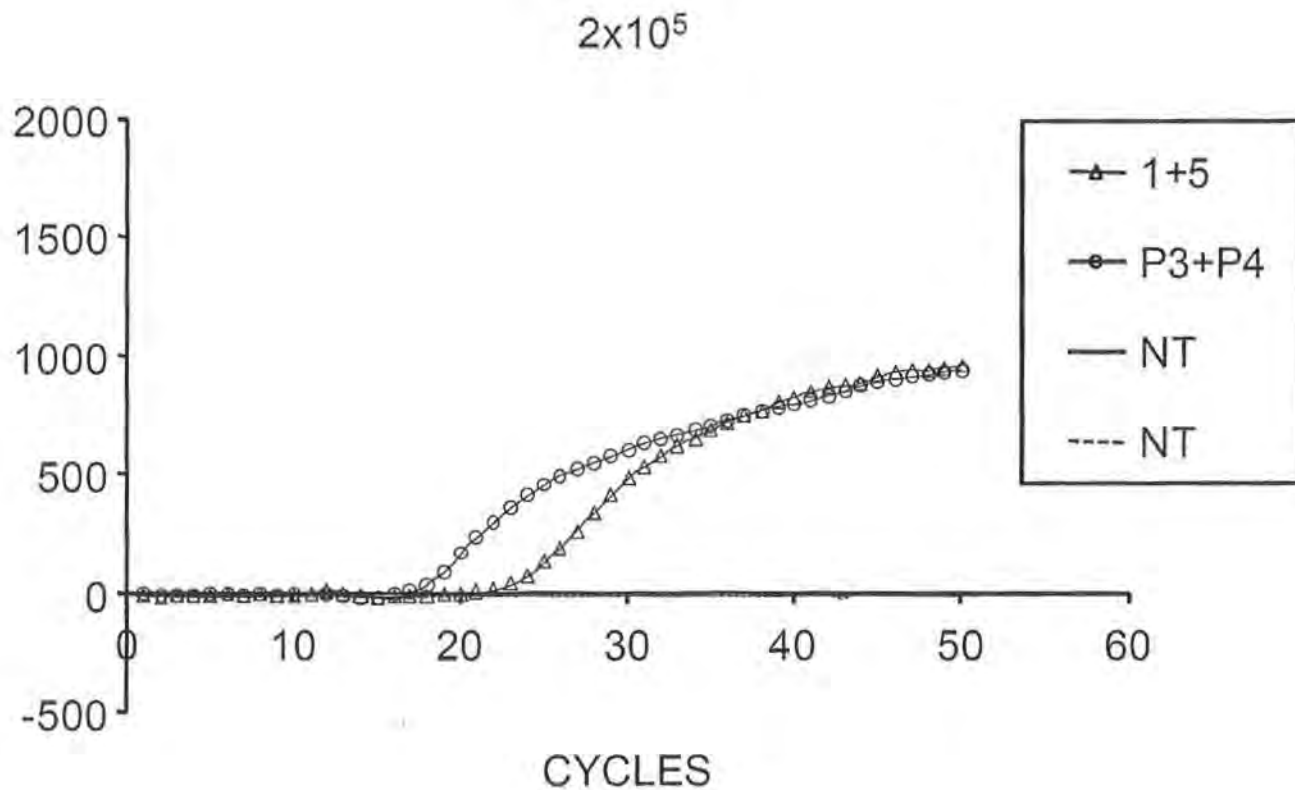


FIG. 7

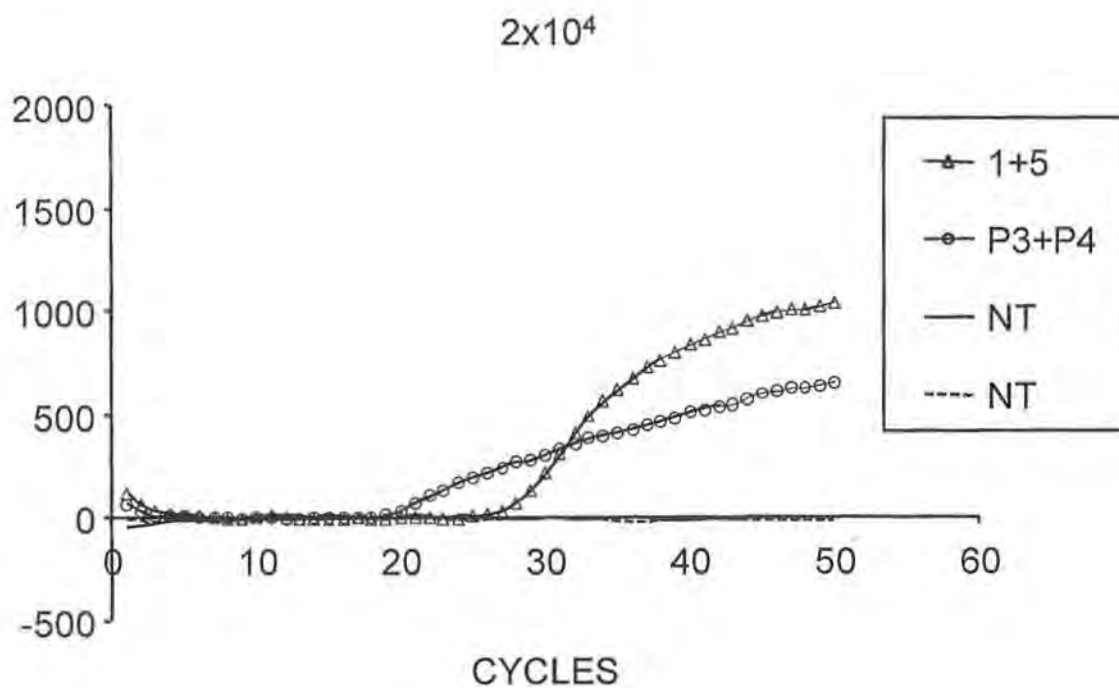


FIG. 8

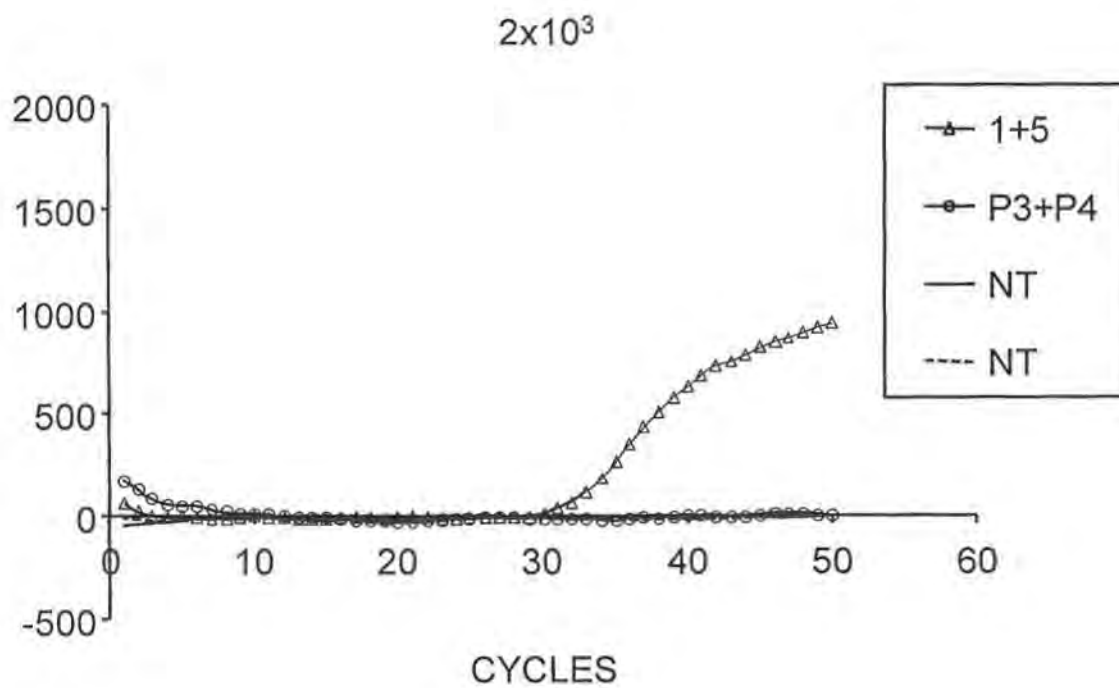


FIG. 9

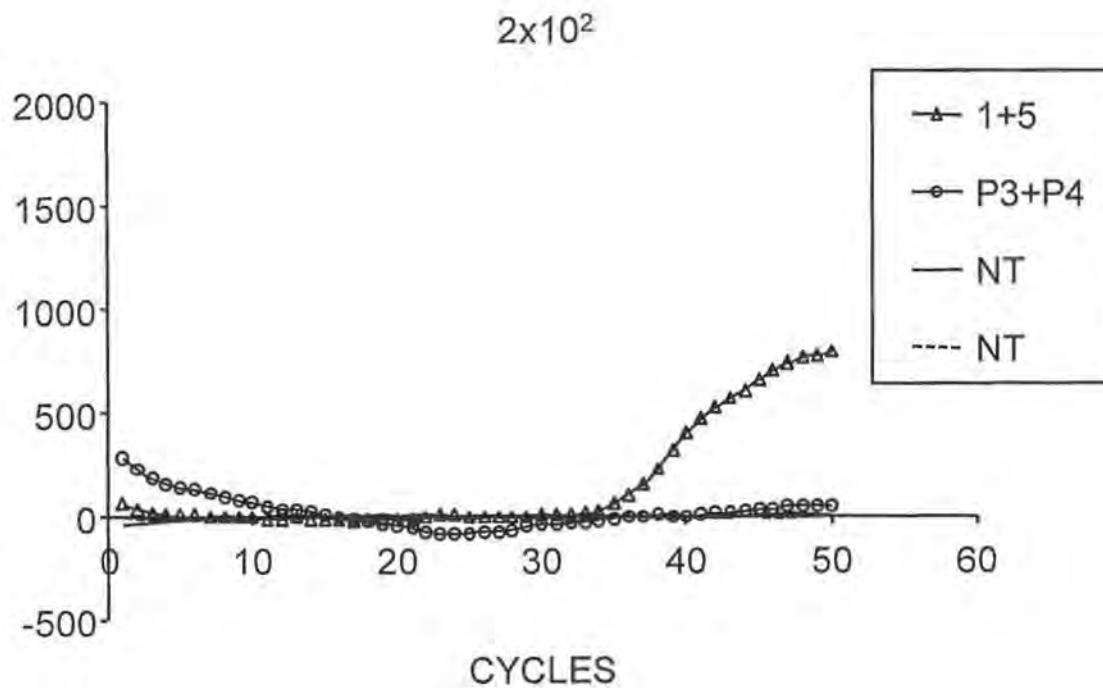


FIG. 10

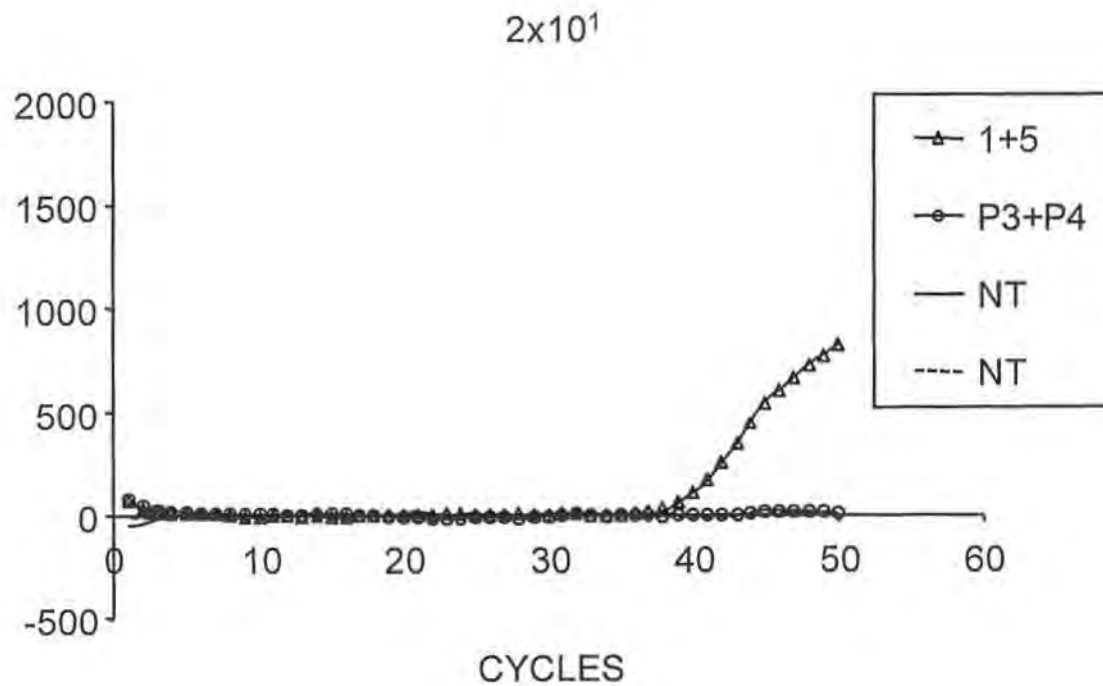


FIG. 11

10. RT-PCR results (500 copies RNA input):

A RT-PCR curve should be interpreted in the same way as a PCR curve. The difference between the two is a pretreatment step in which the RNA target material is reverse transcribed into DNA, which is then used as the input nucleic acid target sequence for the standard PCR reaction.

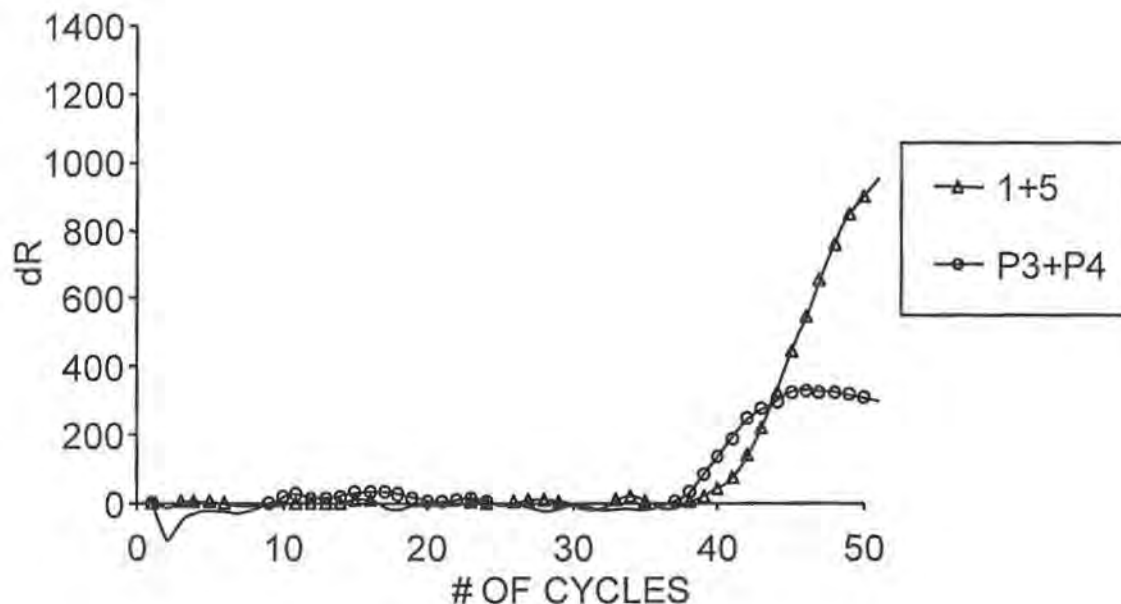


FIG. 12

11. Discussion

In view of the above results, it is clear that the primers of the present invention indeed perform better than the primers of Bell & Ratner, a previously published set of primers targeted to the HIV-1 LTR, thereby providing a more sensitive HIV detection in NASBA, PCR and RT-PCR amplification assays. The primer pair of Bell & Ratner can detect HIV in a NASBA assay only when the viral load is at least 10^4 copies and in a PCR assay only when the viral load is about 2×10^4 copies. In contrast, the primer pair encompassed by the present invention (SEQ ID NOs. 1 and 5) is capable of detecting 2×10^1 copies in PCR and even 10^1 copies in NASBA. Thus, the primer pairs of the claimed invention are about 1000-fold more sensitive than the LTR primer pair of Bell & Ratner. In view of these results, it is clear that not all primers derived from the HIV genome or even those derived only from the LTR have the same sensitivity in amplification assays. The primer pairs of the presently claimed invention provide a clear advantage over other primer pairs derived from the LTR as exemplified by the primer pair of Bell & Ratner, P3 and P4.

12. Second set of NASBA amplification assays

Additional amplification experiments were performed using NASBA that further demonstrate that the primers of the presently claimed invention perform better than other primers developed from the LTR region of HIV-1 (e.g., the primer pair (P3 and P4) disclosed in Bell & Ratner).

A. Reaction mixture:

70 mM KCl
0.2 μ M of each primer
0.1 μ M of LTR-Molecular Beacon
12 mM MgCl₂
2 mM rNTPs
1 mM d NTPs
0.5 mM rITP
15% DMSO
32 units T7 RNA Polymerase
Trehalose
0.08 units RNaseH
6.4 units AMV-RT
5 mM DTT

B. Template material: viral lysate with HIV-1 virus HXB2 nucleotide sequence.

C. Primers (see diagram of primers (Figure 13) below):

Table 1

<u>Primer</u>	<u>Length</u>	<u>Based on</u>	<u>Combined with</u>
5A	22nt	10 nt at 3' end of SEQ ID NO:5	1A, 1B, 1C, P3
5B	20 nt	10 nt at 3' end of SEQ ID NO:5	1A, 1B, 1C, P3
5C	18 nt	10 nt at 3' end of SEQ ID NO:5	1A, 1B, 1C, P3
5D	22 nt	10 nt at 5' end of SEQ ID NO:5	1A, 1B, 1C, P3
5E	20 nt	10 nt at 5' end of SEQ ID NO:5	1A, 1B, 1C, P3
5F	18 nt	10 nt at 5' end of SEQ ID NO:5	1A, 1B, 1C, P3
SEQ ID NO:5	20 nt	SEQ ID NO:5	1A, 1B, 1C, P3
P4 (Bell & Ratner)	30 nt		1A, 1B, 1C, P3

Table 2

<u>Primer</u>	<u>Length</u>	
1A	18 nt	Complete SEQ ID NO:1
1B	26 nt	3' extension of SEQ ID NO:1
1C	26 nt	5' extension of SEQ ID NO:1
P3 (Bell & Ratner)	20 nt	

>>GTAACCACTGCTTAAGCCTCAATAAAGCTTGCTTGAGTGCTTCAAGTAGTGCTGCCGGTCTGTTG>>>TGTGGAAATCTCTAGCACTGGGCGCGAATAGGACCT

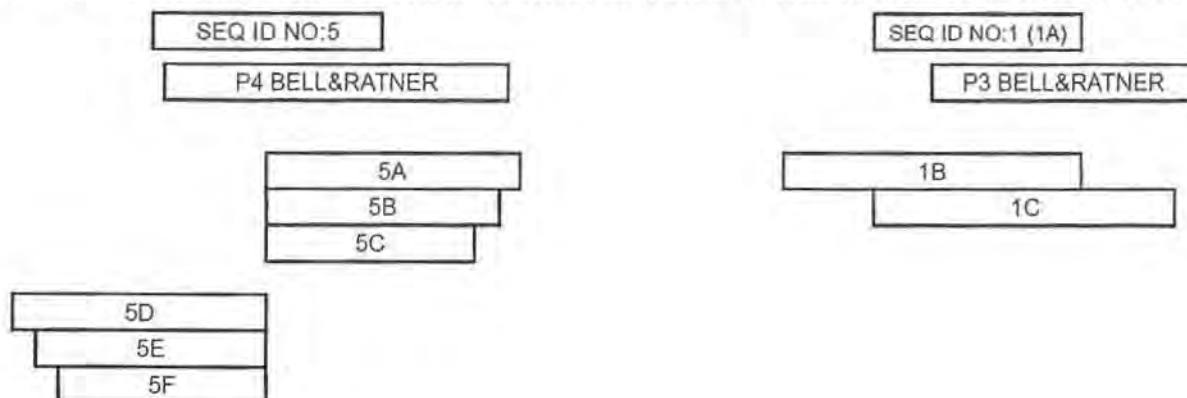


FIG. 13

Each of the primers in Table 1 were tested in a NASBA assay together with a first primer selected from SEQ ID NO:1 (1A), P3 of Bell & Ratner, or the elongated primers, 1B and 1C, which have 26 nucleotides and contain the complete nucleotide sequence of SEQ ID NO:1 (18 nt) plus either 8 nucleotides 3' (1B) or 8 nucleotides 5' (1C). The first primer was provided with an additional T7 promoter sequence.

Primers based on SEQ ID NO:5 were elongated at the 5' end with 12, 10, or 8 nucleotides (5A to 5C) or at the 3' end with 12, 10 or 8 nucleotides (5D to 5F).

The primer pairs were tested with different amounts of template (10^3 , 10^2 , 10^1 , or No Template (NT)).

13. The results of the assays are shown in Figures 14-20, below. In Figures 14-20, the units for the Y-axis are "fluorescence units" and IU refers to "International Units."

SEQ ID NO:5

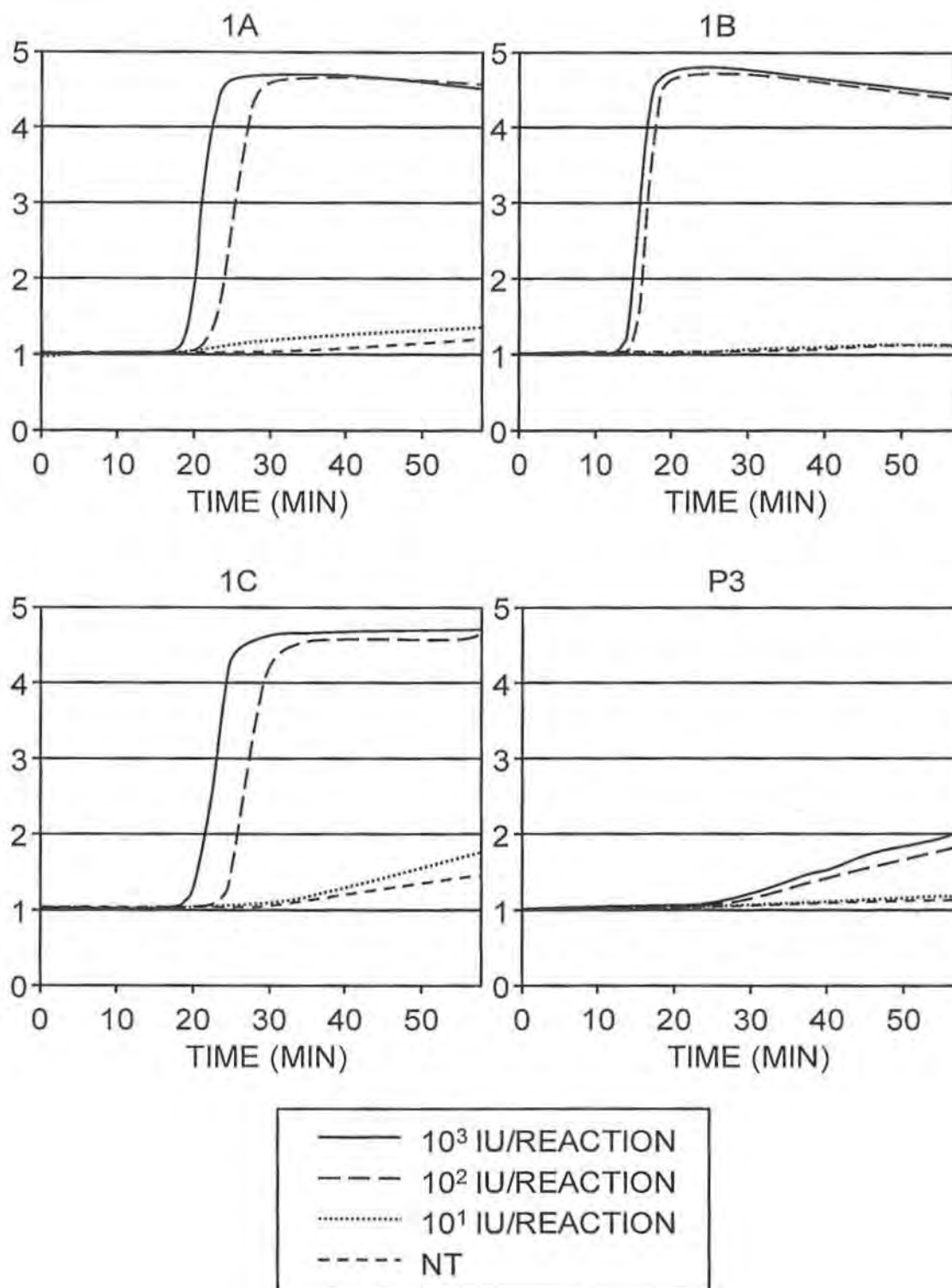


FIG. 14

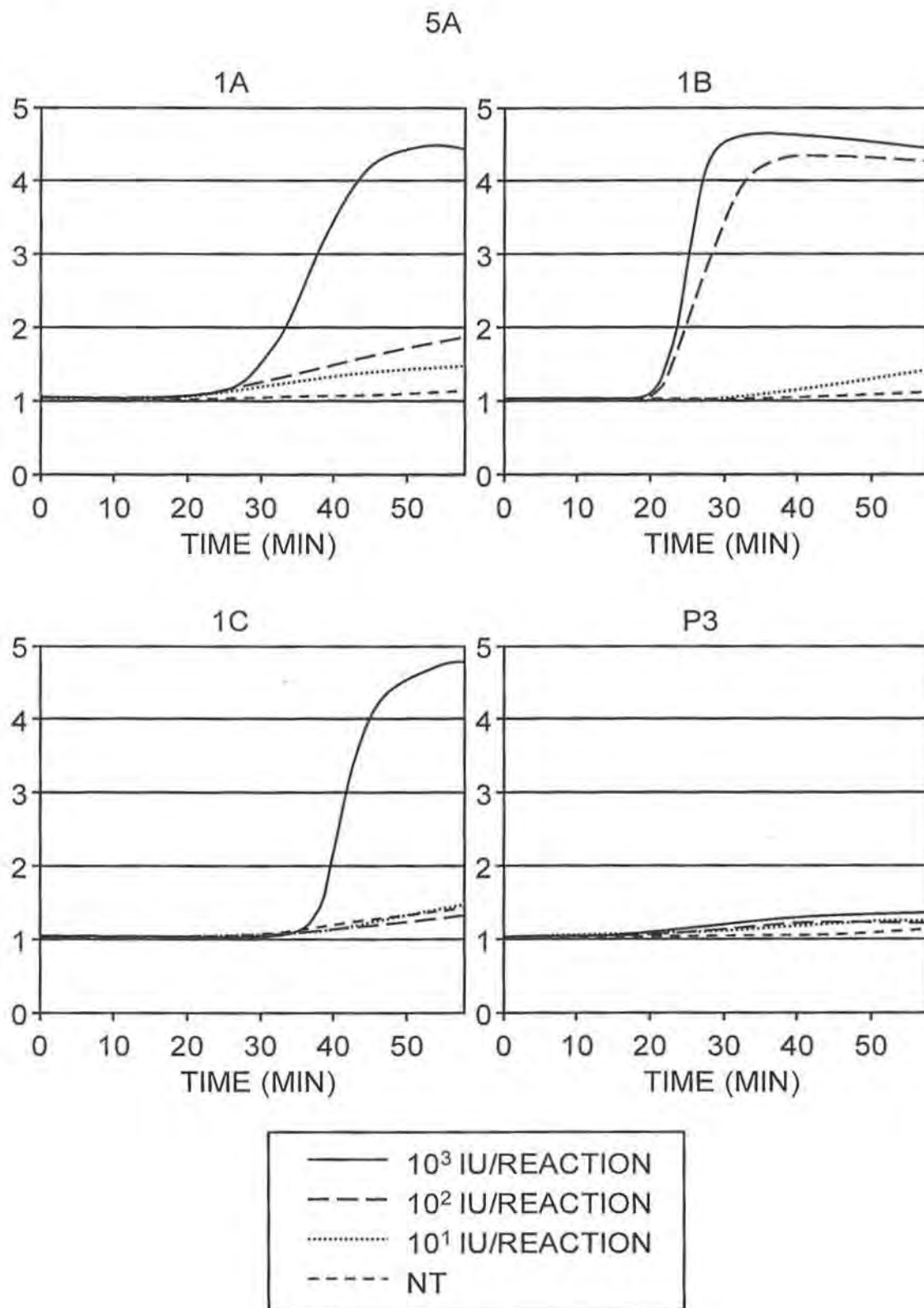


FIG. 15

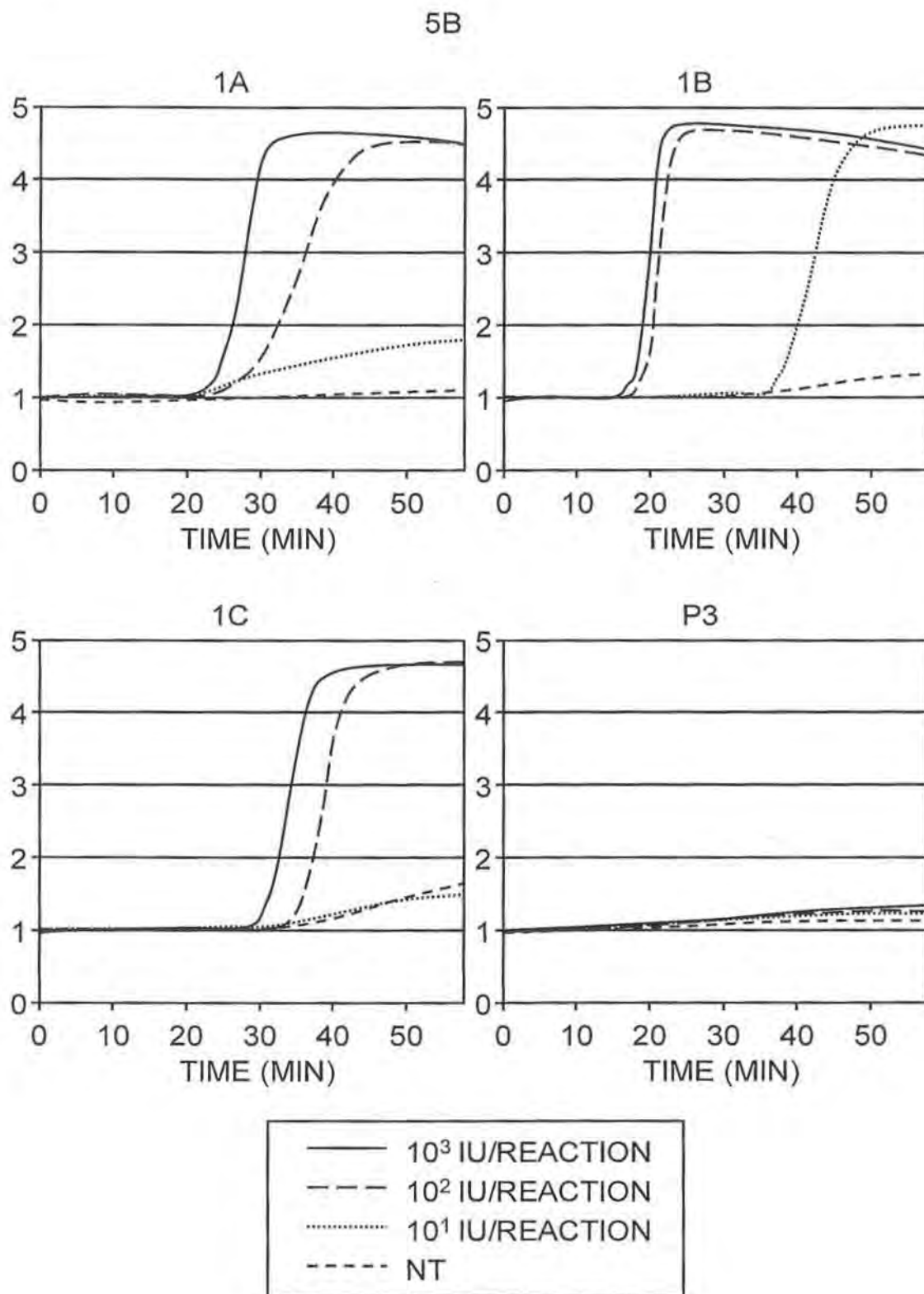
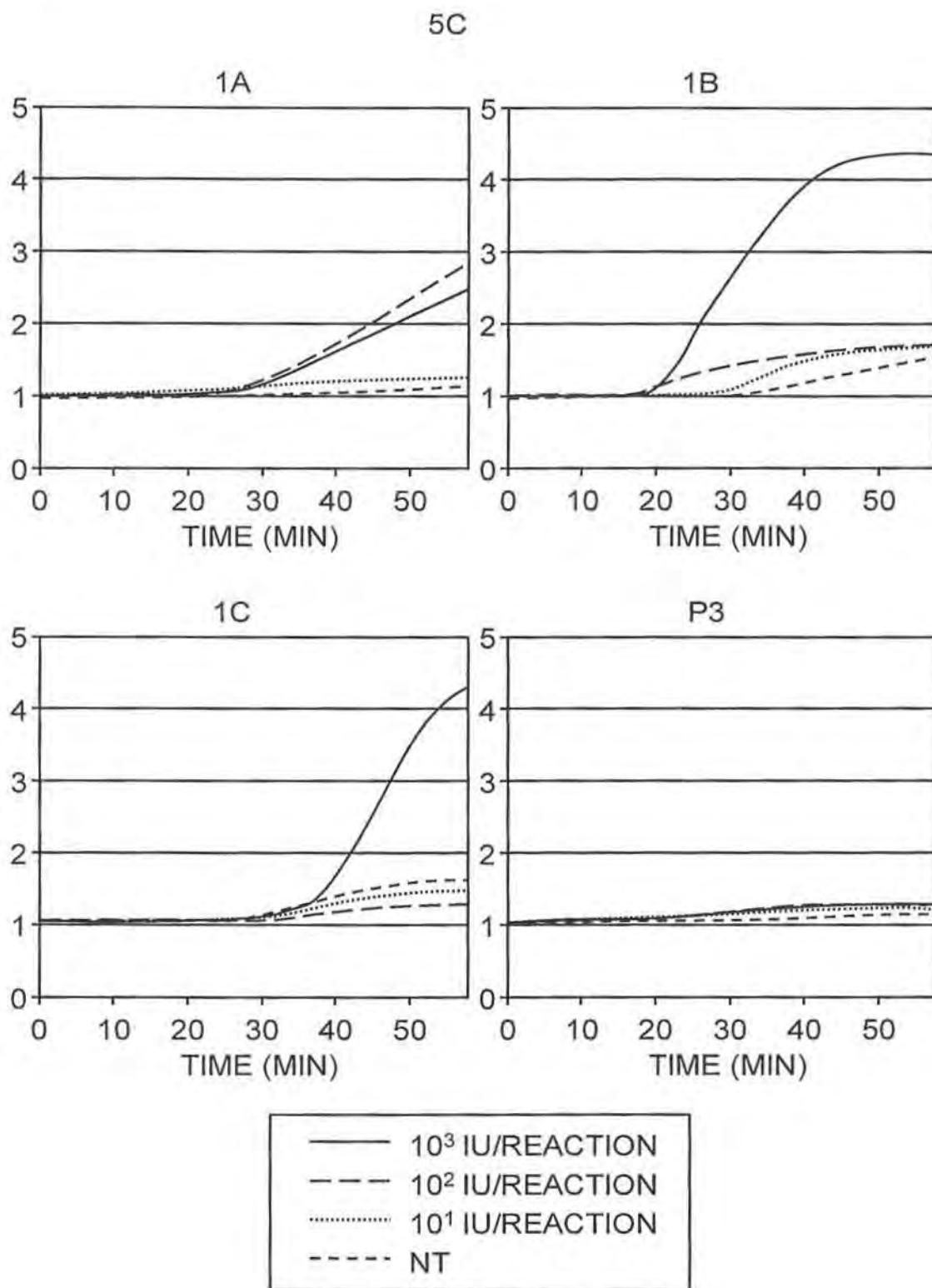


FIG. 16



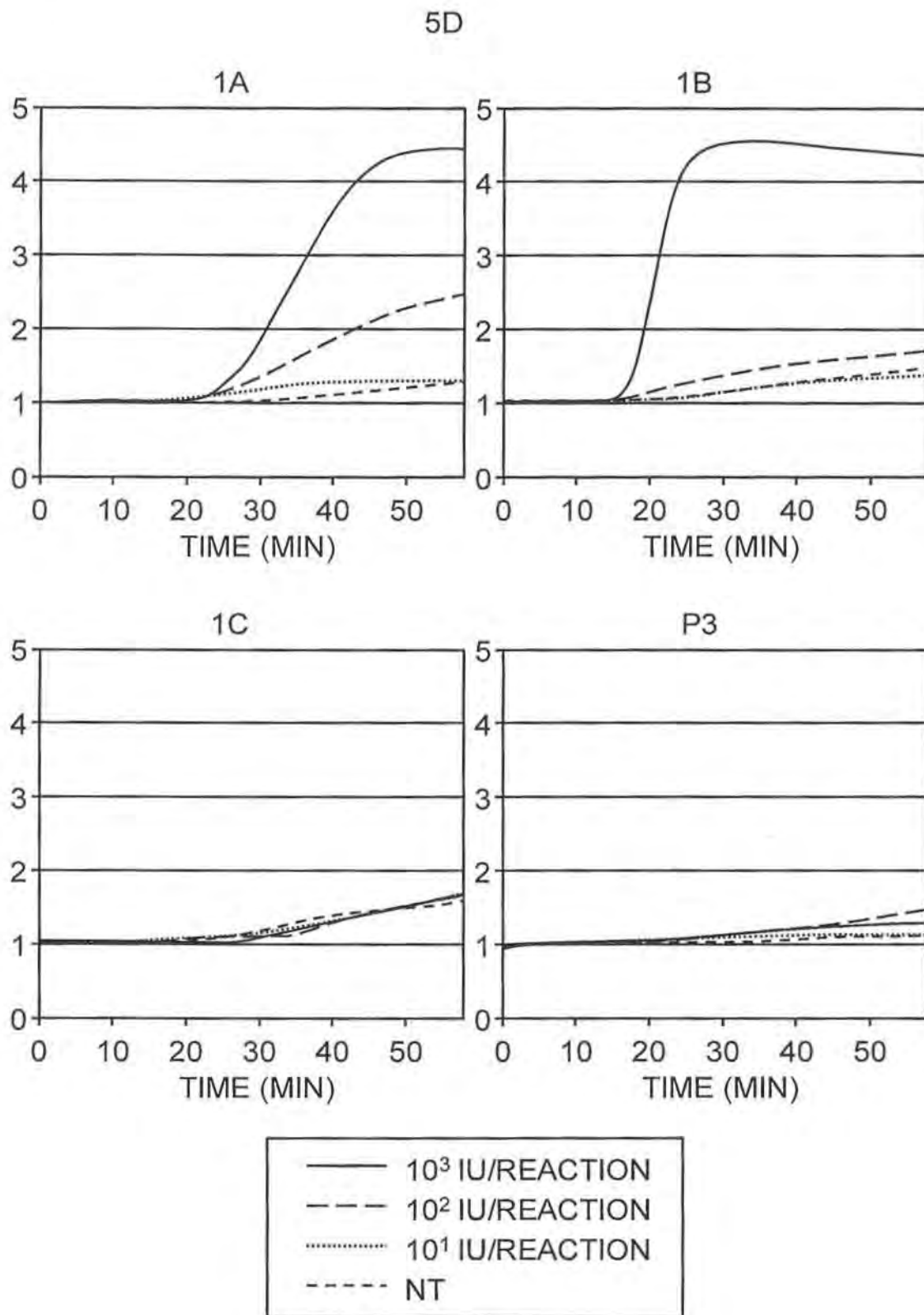
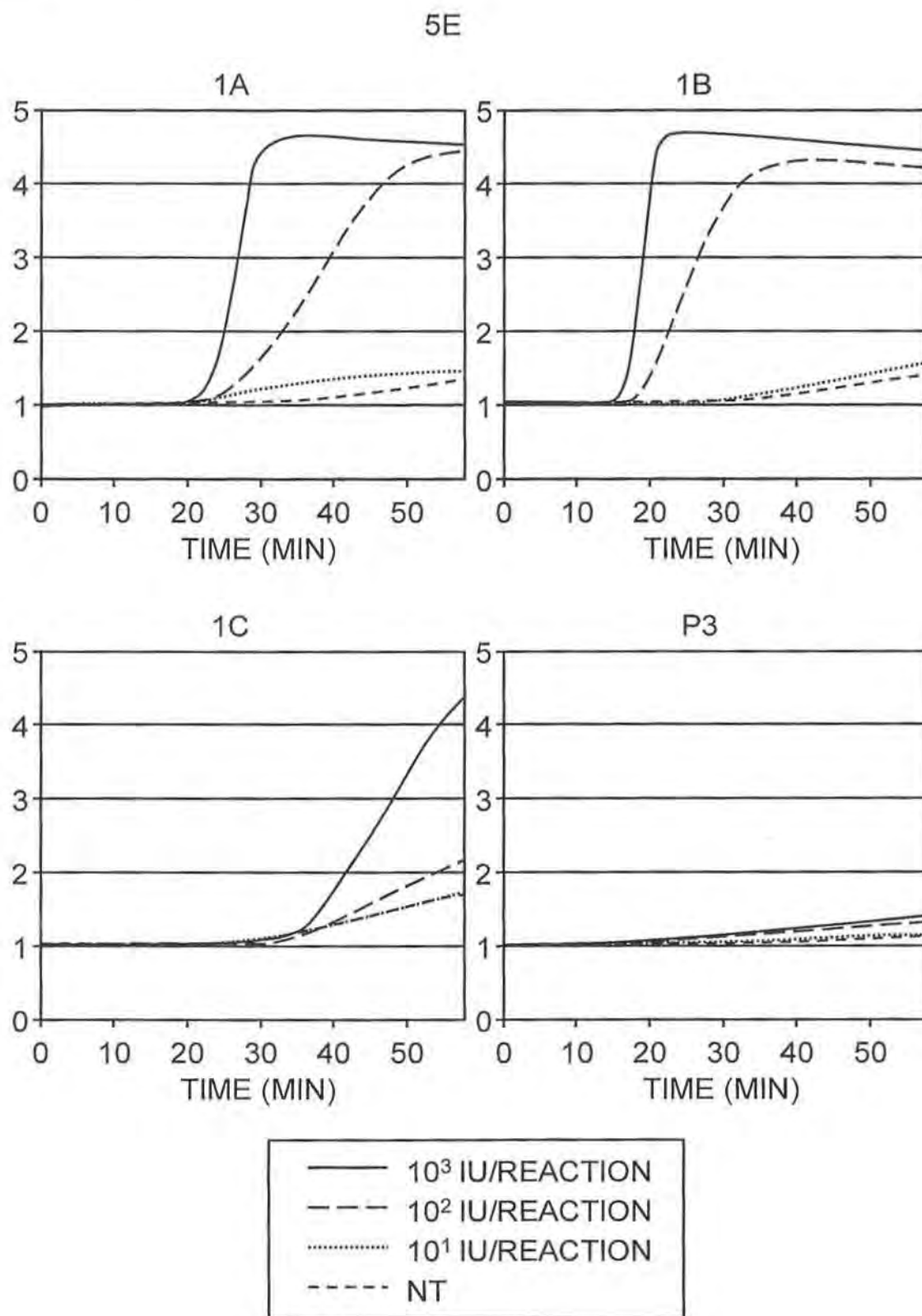
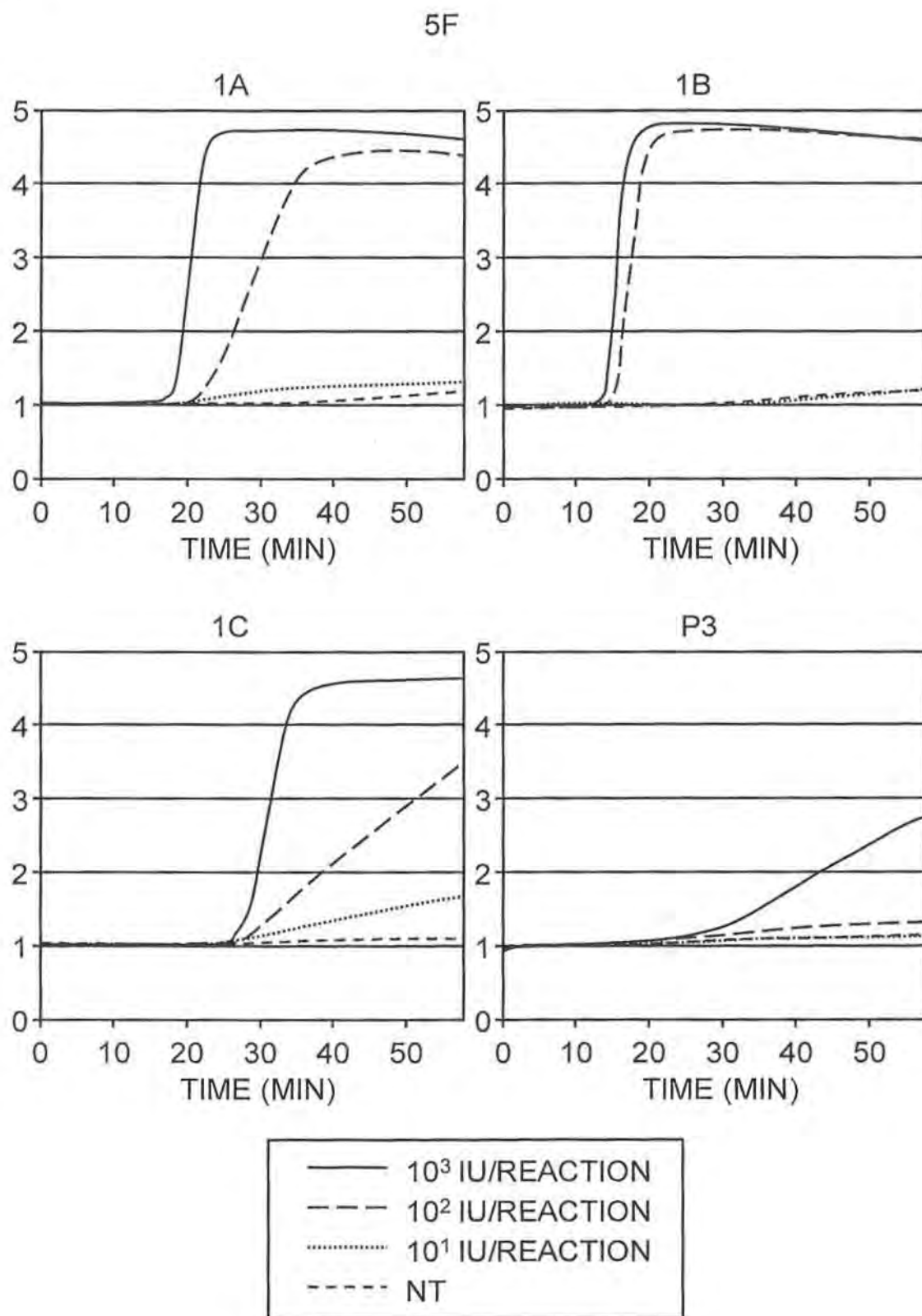


FIG. 18





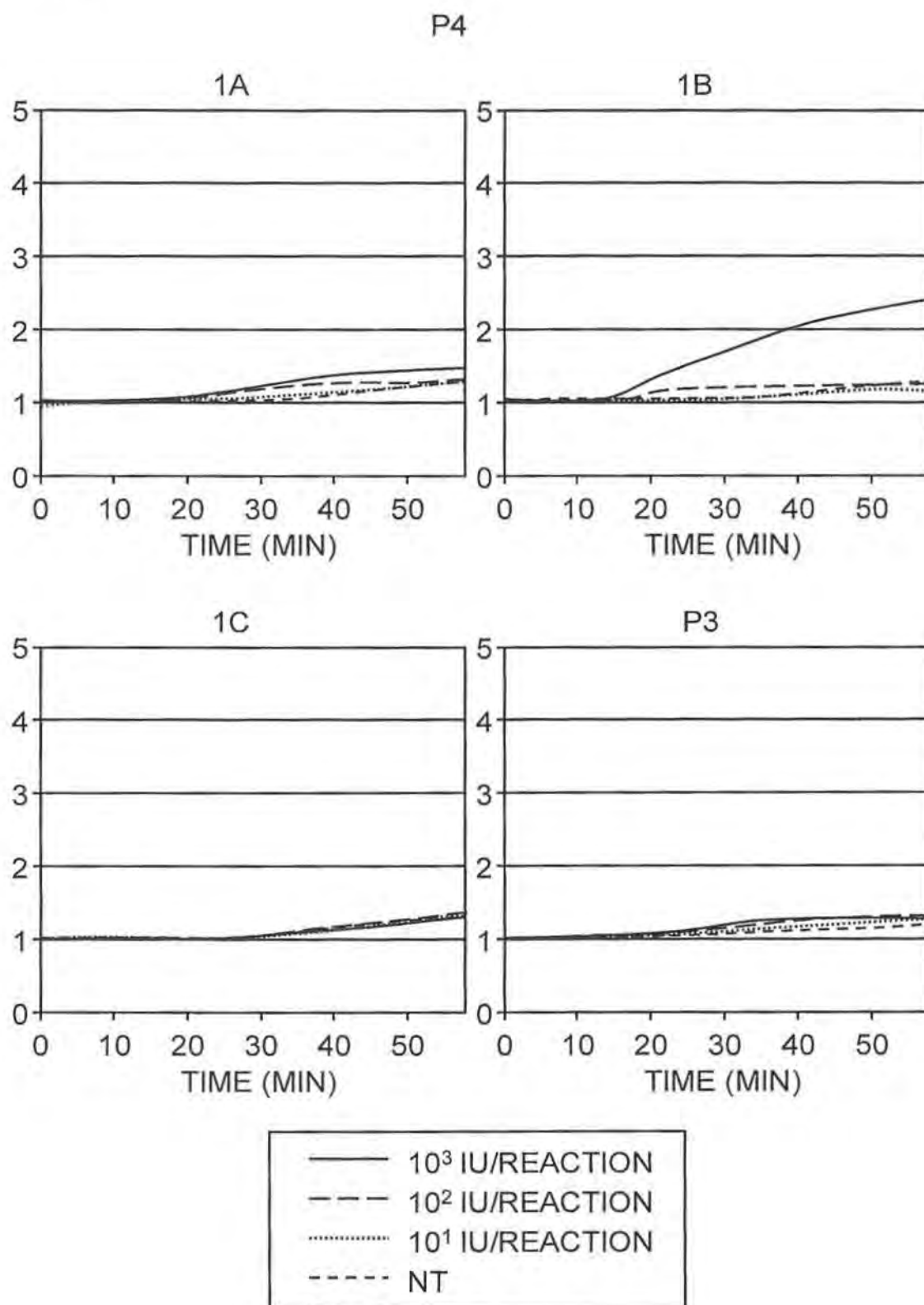


FIG. 21

14. Discussion

From the data shown in Figures 14-21 (sections 12-13 above), it is clear that the primers of the present invention provide unexpectedly better results than that provided by the primer pair of Bell & Ratner (a previous publication disclosing an exemplary set of primers derived from the HIV-1 LTR). The primers of the present invention are consistently more sensitive than those of Bell & Ratner, detecting levels of HIV-1 as low as 10^1 IU/reaction (Fig. 16) and consistently as low as 10^2 IU/reaction (see, Fig. 14, 15, 16, 17, 18, 19, and 20), while the primer pair of Bell & Ratner was unable to detect HIV-1 even at levels of 10^3 IU/reaction (Fig. 21).

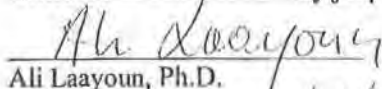
In each case, the primers of the present invention having SEQ ID NO:5 or extensions of 8, 10 and 12 nucleotides at the 5' or the 3' end of SEQ ID NO:5 (5A through 5F), showed greater sensitivity and thus better ability to detect HIV-1 (Figs. 14-20) than the P4 primer of Bell & Ratner when the P4 primer is in combination with the P3 primer of Bell & Ratner (Fig. 21) or a primer of the present invention (1A-1C; Fig. 21). Likewise, the primers of the present invention having SEQ ID NO:1 or extensions of 8 nucleotides at the 5' or the 3' end of SEQ ID NO:1 (1A through 1C), showed greater sensitivity and thus better ability to detect HIV-1 than the P3 primer of Bell & Ratner when the P3 primer is in combination with the P4 primer of Bell & Ratner (Fig. 21) or a primer of the present invention (SEQ ID NO:5 and 5A through 5F; Figs. 14-20).

Even those primer pair combinations of the present invention that do not perform as well as other primer pair combinations of the invention still perform better than the Bell & Ratner primer pair. In each case, under the same conditions, the time to positivity as well as the slope of amplification is better for the primer pairs of the present invention than that observed for the primer pair of Bell & Ratner (Figs. 14-21). Further, the above experiments show that the primer pairs of the present invention perform better than a pair of primers in which one of the primers is a Bell & Ratner primer and the other is a primer of the present invention (P3 in Figs 14-20 and P4 in Fig. 21).

Clearly, the primer pairs of the invention provide an unexpected improvement over the Bell & Ratner primer pair, P3/P4.

These results demonstrate that the primer pairs of the present invention are unexpectedly superior to other primer pairs derived from the LTR of HIV-1 in terms of amplification efficiency and detection sensitivity of HIV-1.

17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Ali Laayoun, Ph.D.

Date June 3, 2013

Tab A

Ali LAAYOUN, PhD

Director of Chemical Research & Analytical Technologies

R&D, Molecular Biology

bioMérieux, sa

Centre Christophe Mérieux

5 rue des berges, 38024- Grenoble

0478875337

0619443958

ali.laayoun@biomerieux.com

Education & Background

1992. PhD in Bio-Organic chemistry, Université J. Fourier de Grenoble, France.

1989. Master in Organic & Physical chemistry Université J. Fourier de Grenoble, France.

Expertise

- Molecular Technologies for in-vitro Diagnostics
- Nucleic acid chemistry
- Labeling & detection technologies
- DNA arrays
- Organic chemistry
- Analytical chemistry

Employment History

2003- now. Director of Chemical Research & Analytical Technologies Department (bioMérieux).
Management of Technology programs: new molecules, analytical approaches and molecular tools for nucleic acid testing and in-vitro diagnostics applications.

2000- 2003. Group leader (bioMérieux).

Development of new and innovative approaches for nucleic acid detection on chips and in homogeneous format for in-vitro Diagnostic applications.

1996-2000. Nucleic acids laboratory manager (bioMérieux).

Nucleic acid chemistry and oligos / probes development and management. Collaboration with academic labs and private companies.

1994-1995. "Assistant Professor" at University of Geneva.

1993-1994. Postdoctoral researcher at City of Hope National Medical Center, Department of Cell & Tumor Biology (Duarte, California).

Human DNA methylation in cancer, mechanisms study using modified synthetic nucleotides and oligonucleotides. I participated to the grant applications and publications writing.

Other Information

- Member of : - American Chemical Society.
 - French Chemical Society.
- EU expert: European Framework Programme for Research, Chemistry Panel
- Presentations at international symposiums.
- Author & Co-author of 32 scientific publications (see the attached list).
- Co-inventor of EP and US patents (see attached list).

List of Publications

- 1 Synthesis of N-acridinyl and N-quinolinyl derivatives of radioprotective aminothiols.
P. Demonchaux, **A. Laayoun**, M. Demeunynck and J. Lhomme. *Tetrahedron*, 1989, 45, 6455-6466.
- 2 Transition state analogs as affinity labels for Human DNA Methyltransferase(s).
D. J. Baker, **A. Laayoun** and S. S. Smith. *Biochemical and Biophysical Research Communications*, 1993, 196, 864-871.
- 3 Design of molecules that specifically recognize and cleave apurinic sites in DNA.
N. Berthet, A. Boudali, J-F. Constant, J-L. Décout, M. Demeunynck, A. Fkyerat, J. Garcia, **A. Laayoun**, P. Michon and J. Lhomme. *Journal of Molecular Recognition*, 1994, 7, 99-107.
- 4 Hydrolysis of 2'-deoxypurine nucleosides. The effect of substitution at C-8 position.
A. Laayoun, J-L. Décout and J. Lhomme. *Tetrahedron Letters*, 1994, 35, 4989-4990.
- 5 Hydrolysis of oligonucleotides containing 8-substituted purine nucleosides. A new route for preparing abasic oligodeoxynucleotides.
A. Laayoun, J-L. Décout, E. Defrancq and J. Lhomme. *Tetrahedron Letters*, 1994, 35, 4991-4994.
- 6 Aminothiols linked to quinoline and acridine chromophores efficiently decrease 8-oxo-2'- deoxy guanosine formation in γ -irradiated DNA.
A. Laayoun, Ce. Coulombeau, J-F. Constant, M. Berger, J. Cadet and J. Lhomme. *International Journal of Radiation Biology*, 1994, 66, 259-266.
- 7 Hypermethylation of telomere-like foldbacks at codon 12 of the human c-Ha-ras gene and the trinucleotide repeat of the FMR-1 gene of fragile X.
S. S. Smith, **A. Laayoun**, R. G. Lingeman, D. J. Baker and J. Riley. *Journal of Molecular Biology*, 1994, 243, 143-151.
- 8 Response of M•HpaII to heteroduplexes.
A. Laayoun, D. J. Baker, J. Riley and S. S. Smith. *Gene*, 1994, 150, 195-196.
- 9 DNA adduct 8-hydroxyl-2'-deoxyguanosine (8-hydroxyguanine) affects function of human DNA methyltransferase.
P. W. Turk, **A. Laayoun**, S. S. Smith and S. A. Weitzman. *Carcinogenesis*, 1995, 16, 1253-1255.
- 10 Hairpins are Formed by the Single DNA Strands of the Fragile X Triplet Repeats: Structure and Biological Implications.
X Chen, S.V.S. Mariappan, P. Catasti, R. Ratliff, R.K. Moyzis, **A. Laayoun**, S.S. Smith, E.M. Bradbury,

and G. Gupta. PNAS 1995; 92, 5199-5203.

- 11 Protection against radiation damage to DNA bases.
A. Laayoun, J. Lhomme, and Cadet. *Radioprotectors: Chemical, Biological and Clinical Perspective*. CRC Press, Boca Raton, U.S.A. (E.A. Bump and K.Malaker ed.), 1998, pp.167-183.
- 12 Methylation of slipped duplexes, snapbacks and cruciforms by human DNA(cytosine-5) methyltransferase.
A. Laayoun and S.S. Smith. *Nucleic Acids Research*, 1995, 23, 1584-1589.
13. Adsorption of single-stranded DNA fragments onto cationic aminated latex particles.
Ganachaud, F., A. Elaissari, C. Pichot, **A. Laayoun**, and P. Cros. *Langmuir*, 1997, 13, 701-707.
14. Conjugation of nucleic acid probes to 6-aminoglucose-based homo- and copolymers. II. Application to diagnostics.
T. Delair, B. Badey, M.H. Charles, P. Cros, **A. Laayoun**, A. Domard, C. Pichot and B. Mandrand.
Polym. Adv. Technol., 1997, 8, 545-555.
15. Stalling of human DNA (cytosine-5) methyltransferase at single-strand conformers from a site of dynamic mutation. M.R, Kho, D.J., Baker, **A. Laayoun**, S.S. Smith. *J. Mol. Biol.* 1998, 275, 67-79.
16. Synthesis and characterization of nucleic acid-(co)polymer conjugates : application to diagnostics.
T. Delair, M.H. Charles, P. Cros, **A. Laayoun**, B. Mandrand, C. Pichot. *Polym. Adv. Technol.*, 1998, 9, 349-361.
17. Synthesis and biological evaluation of nucleoside triphosphates incorporating an oxyamino function for "post-amplification labelling"
Trevisiol, E; Defrancq, E; Lhomme, J; **Laayoun, A**; Hoang, A; Beseme, F; Cros, P. *Nucleosides & Nucleotides*, 1999, 18, 979-980.
18. Synthesis of nucleoside triphosphates that contain an aminooxy function for "post-amplification labelling"
Trevisiol, E; Defrancq, E; Lhomme, J; **Laayoun, A**; Cros, P. *Eur. J. Org. Chem.*, 2000, (1), 211-217.
19. Synthesis of methylketone containing nucleoside triphosphates for RNA labeling.
E. Trévisiol, E. Defrancq, J. Lhomme, **A. Laayoun**, P. Cros. *Tetrahedron*, 2000, 56, 6501-6510.
20. Labeling during cleavage (LDC), a new labeling approach for RNA.
Monnot, V., Tora, C., Lopez, S., Menou, L., and **Laayoun, A.** (2001). *Nucleosides, Nucleotides and Nucleic acids*, 20, 1177-1179.
21. Oligodeoxyribonucleotide Activation with 2,4-Phenylenediisothiocyanate and thier Covalent Grafting onto Amine-Functionalized Latex Microspheres. F. Ganachaud, **A. Laayoun**, C. Chaix, Th. Delair, C. Pichot, A. Elaissari. *J. Dispersion Science and Technology*, 22(5), 473-484 (2001)..
22. Labeling during cleavage of nucleic acids for their detection on DNA chips

- A. Laayoun**, I. Sothier, L. Menou, E. Bernal-Mendez, M. Kotera, C. Bourget, E. Trévisiol, J. Lhomme, and A. Troesch. *Nucleosides, Nucleotides and Nucleic acids*, 2003, 22, 649-652.
23. Aryldiazomethane derivatives as reagents for site specific labeling of nucleic acids at phosphate.
Bourget C, Trévisiol E, Lhomme J, Kotera M, Tora C, Bernal-Mendez E, **Laayoun A**. *Nucleosides Nucleotides Nucleic Acids*. 2003; 22, 1371-1373.
 24. Universal labeling chemistry for nucleic acid detection on DNA-arrays.
Bernal-Mendez E, Tora C, Sothier I, Kotera M, Troesch A, **Laayoun A**.
Nucleosides Nucleotides Nucleic Acids. 2003, 22, 1647-1649.
 25. Aryldiazomethanes for universal labeling of nucleic acids and analysis on DNA chips.
A. Laayoun, M. Kotera, I. Sothier, E. Trévisiol, E. Bernal-Méndez, C. Bourget, L. Menou, J. Lhomme, and A. Troesch. *Bioconjugate Chemistry* , 2003, 14, 1298-1306.
 26. Marqueurs aryldiazométhanes pour la détection des acides nucléiques sur puces à ADN.
A. Laayoun, J. Lhomme, M. Kotera, A. Troesch. (rédigé à la demande de l'éditeur), *L'actualité chimique*, 2003, p.8.
 27. Universal Labeling Chemistry for Nucleic Acid Detection on DNA Chip.
A. Laayoun, E. Bernal-Méndez, I. Sothier, M. Kotera and A. Troesch. *Methods Mol. Biol.* 2004, 288, 241-250.
 28. "Pyrenyldiazomethane, a versatile reagent for nucleotide phosphate alkylation".
M. Kotera, M. -L. Dheu, A. Milet, J. Lhomme and **A. Laayoun**, *Bioorg. Med. Chem. Lett.*, 2005, 705-708.
 29. "Biotin-Phenyldiazomethane Conjugates as Labeling Reagents at Phosphate in Mono and Polynucleotides".
C. Bourget, E. Trévisiol, I. Bridon, M. Kotera, J. Lhomme and **A. Laayoun**, *Bioorg. Med. Chem.* 13, 2005, 1453-1461.
 30. Clip-phen conjugates for the specific cleavage of nucleic acids.
L. Alain, Wright, M, **Laayoun, A**. Tissol, L. and Pitie, M. *Nucleosides Nucleotides & Nucleic acids*, 2007;26(8-9):927-30.
 31. New substituted aryldiazomethyl labels for high density DNA chip-based nucleic acid testing.
Laurent A, Kotera M, Burr A, Lasnet F, Martin T, **Laayoun A**. *Nucleic Acids Symp Ser (Oxf)*. 2008, 253-254.
 32. Rapid real-time nucleic Acid sequence-based amplification-molecular beacon platform to detect fungal and bacterial bloodstream infections.
Zhao Y, Park S, Kreiswirth BN, Ginocchio CC, Veyret R, **Laayoun A**, Troesch A, Perlín DS. *J Clin Microbiol*. 2009, 7, 2067-2078.

Patent Applications

Docket Number	Country	Case Type	Patent Number	Grant date	Application Number	Application Date	Status	Current Owner
00079	JP	Regular	4211948	07/11/2008	JP10507681	01/08/1997	Granted	bioMérieux S.A.
00079	US	Regular	US6537783	25/03/2003	US09214658	01/08/1997	Granted	bioMérieux S.A.
00125	AU	Regular	AU750475	31/10/2002	AU42692/99	17/06/1999	Granted	bioMérieux S.A.
00125	CN	Regular	ZL99809009.3	08/08/2007	CN99809009.3	17/06/1999	Granted	bioMérieux S.A.
00125	FR	Regular	FR9807870	11/10/2002	FR9807870	17/06/1998	Granted	bioMérieux S.A.
00125	FR	Regular	EP/FR1087983	18/03/2009	EP99957062.5	17/06/1999	Granted	bioMérieux S.A.
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00125	US	Regular	US6376179	US09446156	23/04/2002	US09446156	17/06/1999	Granted	bioMérieux S.A.
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Nouvel oligonucléotide marqué								
00434	FR	Regular	FR0653982	12/12/2008	FR0653982	28/09/2006	Granted	bioMérieux S.A.
Nouvelle sonde de détection								
00483	FR	Regular	FR0854549	20/08/2010	FR0854549	04/07/2008	Granted	bioMérieux S.A.

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FEE TRANSMITTAL		Complete if known	
		Application Number	11/108,233
		Filing Date	April 18, 2005
☒ Applicant asserts small entity status. See 37 CFR 1.27.		First Named Inventor	Jaap Goudsmit
☐ Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.		Examiner Name	Bradley L. Sisson
		Art Unit	1634
TOTAL AMOUNT OF PAYMENT	(\$)	Practitioner Docket No.	9310-22CT

METHOD OF PAYMENT (check all that apply)
☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

☒ Deposit Account Deposit Account Number: 500220 Deposit Account Name: Myers Bigel

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

☐ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, except for the filing fee

☒ Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 ☐ Credit any overpayment of fee(s)

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FEE CALCULATION**1. BASIC FILING, SEARCH, AND EXAMINATION FEES** (U = undiscounted fee; S = small entity fee; M = micro entity fee)

Application Type	FILING FEES			SEARCH FEES			EXAMINATION FEES			Fees Paid (\$)
	U (\$)	S (\$)	M (\$)	U (\$)	S (\$)	M (\$)	U (\$)	S (\$)	M (\$)	
Utility	280	140*	70	600	300	150	720	360	180	
Design	180	90	45	120	60	30	460	230	115	
Plant	180	90	45	380	190	95	580	290	145	
Reissue	280	140	70	600	300	150	2,160	1,080	540	
Provisional	260	130	65	0	0	0	0	0	0	

* The \$140 small entity status filing fee for a utility application is further reduced to \$70 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	Undiscounted Fee (\$)	Small Entity Fee (\$)	Micro Entity Fee (\$)
Each claim over 20 (Including Reissues)	80	40	20
Each independent claim over 3 (Including Reissues)	420	210	105
Multiple dependent claims	780	390	195
Total Claims			
-20 or HP = _____ x _____ = _____			
HP = highest number of total claims paid for, if greater than 20.			
Indep. Claims			
-3 or HP = _____ x _____ = _____			
HP = highest number of independent claims paid for, if greater than 3.			

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$400 (\$200 for small entity) (\$100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fee Paid (\$)
_____ - 100 = _____ / 50 = _____ (round up to a whole number) x _____ = _____				

4. OTHER FEE(S)

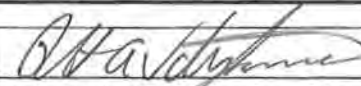
Non-English specification, \$130 fee (no small or micro entity discount)

Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, \$400 fee (\$200 small or micro entity)

Other (e.g., late filing surcharge): Prioritized examination fee

4000.00

SUBMITTED BY

Signature		Registration No. (Attorney/Agent) 50,211	Telephone 919-854-1400
Name (Print/Type)	Robert A. Schwartzman, Ph.D.		Date June 3, 2013

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Electronic Acknowledgement Receipt

EFS ID:	15931868
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Robert Andrew Schwartzman/Marthenn Salazar
Filer Authorized By:	Robert Andrew Schwartzman
Attorney Docket Number:	9310-22CT
Receipt Date:	03-JUN-2013
Filing Date:	18-APR-2005
Time Stamp:	15:21:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Warnings:

Information:

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	Claims		2	6	
	Applicant Arguments/Remarks Made in an Amendment		7	19	
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Total Files Size (in bytes):			4963322		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

**CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION
UNDER 37 CFR 1.102(e) (Page 1 of 1)**

First Named Inventor:	Jaap Goudsmit	Nonprovisional Application Number (if known):	9310-22CT
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i), the prioritized examination fee set forth in 37 CFR 1.17(c), and if not already paid, the publication fee set forth in 37 CFR 1.18(d) have been filed with the request. The basic filing fee, search fee, examination fee, and any required excess claims and application size fees are filed with the request or have been already been paid.
2. The application contains or is amended to contain no more than four independent claims and no more than thirty total claims, and no multiple dependent claims.
3. The applicable box is checked below:

I. ☐ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

- i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.

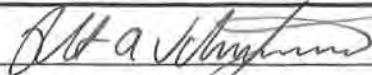
---OR---

- (b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.

- ii. An executed oath or declaration under 37 CFR 1.63 is filed with the application.

II. ☒ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

- i. A request for continued examination has been filed with, or prior to, this form.
- ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
- iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
- iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
- v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature 	Date June 3, 2013
Name (Print/Typed) Robert A. Schwartzman, Ph.D.	Practitioner Registration Number 50211

Note: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required in accordance with 37 CFR 1.33 and 11.18. Please see 37 CFR 1.4(d) for the form of the signature. If necessary, submit multiple forms for more than one signature, see below*.

☒ *Total of 1 forms are submitted.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 11/108,233	Filing Date 04/18/2005	☐ To be Mailed
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ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO**APPLICATION AS FILED – PART I**

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE (\$)	FEE (\$)
☒ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	300
☐ SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 = *		X \$ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 = *		X \$ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	300

APPLICATION AS AMENDED – PART II

AMENDMENT	(Column 1)	(Column 2)	(Column 3)	RATE (\$)	ADDITIONAL FEE (\$)	
	06/03/2013	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		
	Total (37 CFR 1.16(i))	+ 14	Minus	** 25	= 0	X \$80 = 0
	Independent (37 CFR 1.16(h))	+ 3	Minus	***6	= 0	X \$420 = 0
	☐ Application Size Fee (37 CFR 1.16(s))					
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					
					TOTAL ADD'L FEE	0

AMENDMENT	(Column 1)	(Column 2)	(Column 3)	RATE (\$)	ADDITIONAL FEE (\$)	
		CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		
	Total (37 CFR 1.16(i))	+	Minus	**	=	X \$ =
	Independent (37 CFR 1.16(h))	+	Minus	***	=	X \$ =
	☐ Application Size Fee (37 CFR 1.16(s))					
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/GLORIA TRAMMELL/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2

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Doc Code: TRACK1.DENY

**Decision Dismissing Request for
Prioritized Examination (After RCE)**

Application No.: 11/108233

1. THE REQUEST FILED 6/3/13 IS **DISMISSED** BECAUSE:

A. ☐ Request:

- i. ☐ The request was not filed with or after an RCE.
- ii. ☐ The request was filed with or after an RCE, but the RCE was improper.
- iii. ☐ The request was not filed prior to the mailing of a first Office action after the RCE.
- iv. ☐ The application is a utility application, and the request was not filed by EFS-Web.
- v. ☐ A request for prioritized examination after an RCE was previously granted in this application.

B. ☐ Application:

- i. ☐ The application is neither a utility application nor a plant application filed under 35 U.S.C. 111(a) or that entered the national stage under 35 U.S.C. 371, but rather is a _____, which is excluded from the prioritized examination program.

C. ☒ Fees:

One or more of the following fees have not been filed in the application:

- i. ☒ Publication fee, as set forth in 37 CFR 1.18(d).
- ii. ☒ Prioritized examination processing fee, as set forth in 37 CFR 1.17(i).
- iii. ☒ Prioritized examination fee, as set forth in 37 CFR 1.17(c).
- iv. ☐ Excess independent claim fee, due because the number of independent claims exceeds three, as set forth in 37 CFR 1.16(h).
- v. ☐ Excess claim fee, due because the number of claims exceeds twenty, as set forth in 37 CFR 1.16(i).

D. ☐ Claims:

The application contains or has been amended to contain:

- i. ☐ More than four independent claims.
- ii. ☐ More than thirty total claims.
- iii. ☐ One or more multiple dependent claims.

E. ☐ The Prioritized Examination program has exceeded its limit of 10,000 requests for the current fiscal year.

F. ☒ Other: _____

2. CONCLUSION

The application will not undergo prioritized examination. Any further request for prioritized examination will be evaluated for compliance with the above requirements as of the date of its submission.

Telephone inquiries with regard to this decision should be directed to Cheryl Gibson-Baylor at (571)272-3213, Office of Petitions. In his/her absence, calls may be directed to Brian W. Brown, (571)272-5338.

Cheryl Gibson-Baylor
/Cheryl Gibson-Baylor/
[Signature]

Petitions Examiner
(Title)



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814
20792 7590 06/18/2013 MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			EXAMINER SISSON, BRADLEY L	
			ART UNIT 1634	PAPER NUMBER
			MAIL DATE 06/18/2013	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.
11/108,233

Applicant(s)
GOUDSMIT ET AL.

Examiner
Bradley L. Sisson

Art Unit
1634

AIA (First Inventor to File)
Status
No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3 June 2013.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 36,41,46,50,52,53,55,56 and 58-60 is/are pending in the application.
5a) Of the above claim(s) 50,52,53,55 and 56 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 36,41,46 and 58-60 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 07 October 2011 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

- a) ☒ All b) ☐ Some * c) ☐ None of the:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/463,352.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Interim copies:

- a) ☐ All b) ☐ Some c) ☐ None of the: Interim copies of the priority documents have been received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: ____
- 4) ☐ Other: ____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 June 2013 has been entered.

Election/Restrictions

2. Claims 50, 52, 53, 55, and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on -5 November 2007.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/463,352, filed on 21 January 2000.

Drawings

4. The drawings were received on 07 October 2011. These drawings are acceptable.

Terminal Disclaimer

5. The terminal disclaimer filed on 26 May 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent Application 11/372,577 has been reviewed and is accepted. The terminal disclaimer has been recorded.

6. The terminal disclaimer filed on 01 May 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent 6,881,537 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter because the claimed invention is directed to a naturally-occurring nucleic acid or fragment thereof, whether isolated or not, that is not patent-eligible pursuant to the Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.* --U.S.-- (June 13, 2013).

9. In the particular case, applicant is claiming "oligonucleotide primers for the amplification of a target sequence between two primer binding sites within the LTR region of HIV-1 genome." As specified by the claim, the two primers are to comprise "a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur...[and] said second primer

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comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur.”

10. Acknowledgement is made that the primer is to comprise nucleotides as depicted in SEQ ID NOs. 1 and 5, and that said sequences are DNA whereas HIV-1 is a retrovirus, that is, it comprises RNA not DNA. The fact that the sequence comprises DNA and not RNA does not render the claimed subject matter patent eligible as it is recognized that, with HIV-1 being a retrovirus, it naturally carries/comprises reverse transcriptase so to naturally produce a proviral sequence, which is DNA. Accordingly, the primer sequences, even if construed as being DNA, is still considered to be a naturally-occurring sequences and, thusly, not patent-eligible subject matter.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
14. Claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of US Patent 5,413,906 (Eberle et al.), EP 617132 A2 (McDonough et al.), US Patent 6,001,558 (Backus et al.), US Patent 5,472,840 (Stefano), and applicant's admissions.
15. Attention is directed to MPEP 706.02 [R-9]:

III. RELIANCE ON ADMITTED PRIOR ART IN SUPPORT OF REJECTION

A statement by an applicant in the specification or made during prosecution identifying the work of another as "prior art" is an admission which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988). See MPEP § 2129 for discussion on admissions as prior art. Where the admitted prior art anticipates the claim but does not qualify as prior art under any of the paragraphs of 35 U.S.C. 102, the claim may be rejected as being anticipated by the admitted prior art without citing to 35 U.S.C. 102.

16. Attention is directed to MPEP 2129 [R-6], Admissions as Prior Art, which states in part:

I. ADMISSIONS BY APPLICANT CONSTITUTE PRIOR ART

Art Unit: 1634

A statement by an applicant >in the specification or made< during prosecution identifying the work of another as “prior art” is an admission **>which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988).

17. Attention is also directed to *Ex parte Shirley*, (BPAI, 2009) Appeal No. 2009002352, which, at pages 21 and 26, states:

The Specification’s omission of the term “prior art” and inclusion of the prior-art disclaimer may initially appear to indicate that Appellants do not consider the single-step soft bake process to constitute prior art. To place these latter, contraindicative factors into the proper context though, we note that patent-application drafters regularly endeavor to avoid the indiscriminate or imprudent use of the descriptive label, “prior art.” See *Riverwood Intern. Corp. v. R.A. Jones & Co., Inc.*, 324 F.3d 1346, 1354 (Fed. Cir. 2003) (citing *In re Fout*, 675 F.2d 297, 300 (CCPA 1982)) for the proposition that “section 102 is not the only source of ... prior art. Valid prior art may be created by the admissions of the parties”; *In re Nomiya*, 509 F.2d 566, 571 (CCPA 1975) (holding that an Applicant’s labeling of certain figures as “prior art,” *ipsissimis verbis*, constituted an admission that the pictured subject matter was prior art relative to Applicant’s invention); MPEP § 21294 (instructing that “the examiner must determine whether the subject matter identified as ‘prior art’ is applicant’s own work, or the work of another. In the absence of another credible explanation, examiners should treat such subject matter as the work of another”).

The Specification’s omission of the term “prior art” and inclusion of the boilerplate prior-art disclaimer do not change our conclusion. In view of the record as a whole, these factors are ineffective in shielding Appellants from having their prior-art admissions treated as such.

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18. Attention is directed to MPEP 904.01.

The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

19. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

20. Claims 36, 41, and 46 are independent. Claim 36 is deemed representative and, for convenience, is reproduced below.

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36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer is a maximum of 50 nucleotides in length and comprises (1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15-40 nucleotides in length and comprising at least 15-40 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; and

(2) a promoter operably-linked to said first oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

21. Upon review of the instant disclosure it is noted that there is no part of the disclosure that is labeled as being directed to "Prior Art," or that any of the cited documents constitute "prior art." However, the instant disclosure has been found to specifically identify documents that were published prior to the effective filing date of the subject application. Such documents and applicant's characterization as to what they disclose are considered to be admissions as to prior art. Additionally, a review of the disclosure has also found statements by applicant as to what was known in the art at the time of the invention. Such statements are also considered to be admissions of prior art.

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22. Applicant, at page 2 of the disclosure admits:

Some regions are more prone to sequence variation than others. Especially in the *env* domain sequence variation can be as high as 30% between members of the different subtypes. Ideally, primer selection should be based on knowledge of interstrain variability in candidate primer sequences and the consequences of mismatching at primer sites. McCutchan et al, J.AIDS, 4, 1241-1250, 1991, used PCR to make a genetic comparison of different HIV-1 isolates. Using anchored PCR (varying sense primers were used with a constant antisense primer, primers were chosen from relatively conserved regions in gag, env and LTR)

23. Upon review of the above statement, it is not clear if the characterization of the percent variability of the *env* gene is an admission of prior art or whether it is information obtained by applicant. In answering this question, it is noted that US Patent 4,772,547 (Heimer et al.), which was published nearly 9 years prior to the effective filing date of the subject application, teaches in column 5, third paragraph, that the variability of the *env* gen can be as much as 20 %. Additionally, US Patent 4,963,532 (Carter), which issued 16 October 1990, nearly 7 years prior to the effective filing date of the subject application, states in column 1, lines 32-34: "The most variable region of the HIV genome is the envelope (*env*) gene..." In view of the state of the art at the time of filing, these statements are deemed to be admissions of prior art.

24. Applicant, at page 2, last paragraph, bridging to page 3, of the disclosure states:

Research aimed at identifying suitable primer sets for the reliable amplification of HIV-1 derived nucleic acid sequences has been ongoing for the past years. Engelbrecht et al., *J. Virol. Meth.*, 55, 391-400, 1995, describe a study aimed at the development of a specific and sensitive PCR protocol using *env*, *gag* and LTR primer pairs to detect subtypes present in the Western Cape, South Africa. Twenty four strains of which it was known that they belonged to subtypes B, C and D were analyzed.

25. Applicant, at page 3, last paragraph, admits:

Various techniques for amplifying nucleic acid are known in the art.

26. Montagnier et al., column 1, states:

Acquired immune deficiency syndrome (AIDS) is a condition which is now of major importance in North America, Europe, and Central Africa. The causal agent of AIDS is believed to be a retrovirus. Recent estimates suggest that approximately 1 million Americans may have been exposed to the AIDS virus. The individuals affected show severe immunosuppression, which may be followed by the onset of fatal diseases.

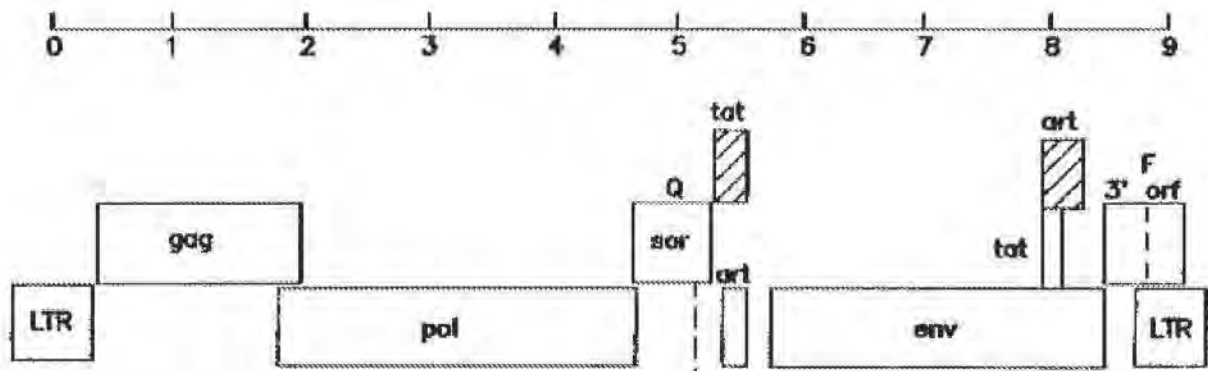
It is now universally recognized that viruses previously denominated lymphadenopathy associated virus (LAV), immune deficiency associated virus (IDAV1 and IDAV2), human T-lymphotropic virus type III (HTLV-III), and AIDS related virus (ARV) are all variants of the same retrovirus. See, *e.g.*, Nature, 313:636-637 (1985).

A subcommittee empowered by the International Committee on the Taxonomy of Viruses recently proposed that the AIDS retroviruses be officially designated as the "Human Immunodeficiency Viruses," to be known in abbreviated form as "HIV."

Montagnier et al., column 2, states:

Moreover, there are compelling epidemiological considerations that make early detection of infection by the AIDS virus essential. Thus, for example, infection of an individual with the AIDS virus may be suspected because of the clinical symptoms manifested by the individual, but the infection may be in a very late stage before these symptoms are observed. Meanwhile, transmission of the disease may have taken place.

27. The structure/organization of the nucleotide sequence of HIV-1 as well as the nucleotide sequence of same are known in the art at the time of filing. Montagnier et al., in Figure 1, presents a graphic showing the relative size of the genome in kilobases as well as its organization.



As is readily apparent from the cropped image of FIG. 1, *supra*, the genetic organization of HIV-1 comprises a Long Terminal Repeat (LTR) region on both ends of the genome, and that the relative size of the LTR regions constitute but a very small segment of the genome.

28. While Montagnier et al., do teach of serologic testing and the polypeptides and antibodies that could be used in such methodologies, they unequivocally consider polynucleotides, such as primers, to also be part of their invention. In support of this position, attention is directed to column 18 where Montagnier et al., refer explicitly to “polynucleotides of the invention.”

29. Montagnier et al., provide motivation for the selection and use of primers for the detection of HIV-1 infected individuals were at column 18, bridging to column 19, Montagnier et al., teach that a PCR assay can be conducted in “less than three days” and can be used to detect HIV provirus (the cDNA copy of the RNA of the HIV-1 genome that has integrated into the chromosomes of the host (human) cell). In comparison, a serologic “procedure can take up to three to four weeks and lacks sensitivity in that viruses cannot be consistently isolated from persons with documented infections.” Such explicit statements by Montagnier et al., clearly provides motivation to one of skill in the art to develop primers that can be used to detect HIV-1 infection in an individual not only in a considerably faster method, but also in a more sensitive

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approach in that the virus can be detected before the patient expresses virus or produces any antibodies against the virus.

30. Montagnier et al., column 19, bridging to column 20, teach of the potential that any given individual may have been exposed to HIV-1 with genetic variations, and that detection of the particular variant(s) of HIV-1 that an individual has been exposed to “is preferably carried out” using primers and probes “derived from highly conserved regions of the viral genome, such as the LTR...”

31. As set forth above, Montagnier et al., clearly recognize the need, if not urgency, in developing a faster and more sensitive assay, that PCR would provide such a detection mechanism, and then directs one of skilled in the art to not only the specific region of the HIV-1 genome, but also further directs one to develop primers that correspond to “highly conserved regions” of the LTR.

32. Applicant, at page 8 of the disclosure, teaches that the primers/oligonucleotides are “substantially complementary to a sequence of the LTR region of a nucleic acid sequence of a HIV genome.” Nucleic acids corresponding to SEQ ID NO: 1 and 5 are specifically identified. This is the very region that Montagnier et al., explicitly directs one of skill in the art to go to and select primers

33. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007);

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the

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anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

34. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes "background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ," *KSR* at 1396. In demonstration of the "specialized understanding of one of ordinary skill in the art, and the common understanding of the layman," it is noted that STN Registry No. 11793-79-3 discloses the nucleotide sequence of the LTR of HIV-1.

35. Suggestion, teaching or motivation does not have to be explicit and "may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself" *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

36. In the present case, the prior art clearly establishes that there were design pressures and market needs for primers that would allow for the detection of HIV-1 genome via PCR. The prior art also clearly establishes that the structure and nucleotide sequence of the HIV-1 genome was known- including the propensity of numerous variants to develop. The prior art also explicitly directs one of skill in the art to select primers not only from the LTR region of HIV-1, but also from those regions that are "highly conserved." With the prior art teaching one to focus on such a small area, "there are a finite number of identified, predictable solutions."

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37. Montagnier et al., do teach the development of primers from LTR region of HIV-1, and that these primers are to be used in polymerase chain reaction (PCR), the very use that applicant has disclosed. Accordingly, the selection of size of primer size (15-26 nucleotides for the “first oligonucleotide” component of the first primer, and 10-26 nucleotides for the “second oligonucleotide” of the “second primer” (claims 36, 41, 46) and 15-26 nucleotides for the “second oligonucleotide” of the “second primer” (claims 58-60) is deemed to be a matter of obvious design choice for as the instant application does not present any showing that the claimed primers have any unexpected property or yield any unexpected result when used.

38. Attention is directed to MPEP 2112 [R-3]:

The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. “The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness.” *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references).

In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that “just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.” *Id.*

MPEP 2112 II:

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) (“[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.”)

39. Montagnier et al., has not been found to disclose coupling a primer to a promoter nucleotide sequence (limitation of independent claims 36, 41, 46).

40. Eberle et al., column 14, disclose primers directed to LTR of HIV-1. As can be seen therein, the disclosed primer (SEQ ID NO. 1) is 18 nucleotides in length. Also, the primer of Eberle et al., shares the nucleotides GGGCGCCA with that of the instant SEQ ID NO. 1.

41. Eberle et al., has not been found to disclose using additional sequences of LTR, or the inclusion of a T7 promoter sequence coupled to the primer.

42. McDonough discloses in their SEQ ID NO. 50 the complete nucleotide sequence of applicant's SEQ ID NO. 1. As can be seen, SEQ ID NO. 50 contains an additional 4 nucleotides at the 5' terminus and an additional nucleotide at the 3' terminus. By comparison, applicant's first and second primers have been amended such that they no longer have any upper limit. In support of this position, it is noted that claim 36 recites that the "first primer comprises a first oligonucleotide" and that the second primer "comprises a second oligonucleotide." There is no restriction as to the number of additional "oligonucleotides" (or any other component) that each primer can "comprise" so long as it is still functional. Additionally, it is noted that the "first oligonucleotide" of the "first primer" can be 26 nucleotides in length and have but 15 nucleotides corresponding to HIV-1 LTR sequence. Given such, the remaining 11 nucleotides are undefined. Recognizing that each of these undefined 11 positions can be occupied by any one of the four common dNTPs, there are 4^{11} , or 4,194,304 different possible sequences for just these 11 positions when present in a continuous series. In the case of the "second primer" whose oligonucleotide can also be 26 nucleotides in length yet only have 10 sequential nucleotides of

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the SEQ ID NO: 5, there are some 4^{16} , or 4,294,967,296 different primers where all 16 of the undefined positions occur consecutively.

43. Backus et al., disclose an HIV-1 LTR primer, their SEQ ID NO: 2, which is some 30 nucleotides in length and comprises all of applicant's SEQ ID NO: 5. Additionally, SEQ ID NO: 4 of Backus et al., which comprises some 23 nucleotides, comprises the full length SEQ ID NO: 1 claimed instantly, which by way of comparison, is 18 nucleotides in length. It is further noted that the 3' nucleotide sequence of the prior art SEQ ID NO: 4 is the same as the 3' sequence of applicant's SEQ ID NO: 1. Given such explicit teachings, it is clearly evident that the prior art not only fairly points the skilled artisan to the conserved regions of the LTR of HIV-1, but also specifically identifies the same nucleotide sequence for use as a primer.

44. Backus et al., have not been found to teach incorporating a promoter into the primer.

45. Stefano, column 30, teaches the ligation of a T7 promoter sequence to an HIV oligonucleotide/primer. Such a showing meets a limitation of independent claims 36, 41, and 46.

46. Independent claims 36, 41, and 46 require the primers to further comprise a promoter region, which in dependent claims 38, 42, and 48 is limited to "a T3, T7, or SP6 promoter."

47. Applicant, at page 4 of the disclosure, admits:

Another technique for the amplification of nucleic acid is the so-called transcription based amplification system (TAS). The TAS method is described in International Patent Appl. no. WO 88/10315. Transcription based amplification techniques usually comprise treating target nucleic acid with two oligonucleotides one of which comprises a promoter sequence, to generate a template including a functional promoter. Multiple copies of RNA are transcribed from said template and can serve as a basis for further amplification.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295. EP 408295 is primarily concerned with a two-enzyme

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transcription based amplification method. Transcription based amplification methods, such as the NASBA method as described in EP 329822, are usually employed with a set of oligonucleotides, one of which is provided with a promoter sequence that is recognized by a DNA dependent RNA polymerase such as, for example, T7 polymerase. Several modifications of transcription based techniques are known in the art.

In contrast to RT-PCR, NASBA, which is based on RNA transcription by T7 RNA polymerase (Kievits et al., 1991; Compton, 1991), does not need differentiation between RNA- and DNA- derived amplification products since it uses RNA as its principal target. NASBA enables specific amplification of RNA targets even in a background of DNA.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295... One or more "promoter-primers" (oligonucleotides provided with a promoter sequence) may be used in transcription based amplification techniques, optionally combined with the use of one or more oligonucleotides that are not provided with a promoter sequence. For RNA amplification, a transcription based amplification technique, is a preferred technology.

In each of the above-reproduced paragraphs, applicant has provided a summary of the disclosures of the various documents. Such statements, while not labeled as "prior art," are considered to be admissions of prior art.

48. In view of the admitted state of the art where primers comprising a promoter region, such as T7, are used in transcription-based amplification methods, and that the inclusion of the T7 promoter in such primers was known in the art, and that NASBA does not need differentiation between RNA- and DNA-derived amplification products, one of ordinary skill in the art at the time of the invention would have been motivated to have included just such a promoter on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences, be they RNA as found in the viral particles, or DNA, as is found when HIV-1 has integrated into a hosts genome (proviral sequence).

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49. As set forth above, the prior art clearly provides motivation for one of skill in the art to produce useful primers that would allow for the amplification of HIV-1 sequences, and directs the public to select primers from the LTR region of HIV-1. And as seen above, Backus et al., actually discloses primers that comprise the nucleotide sequence of applicants' SEQ ID NO: 1 and 5. The rejection has sets forth that the number of choices confronting the skilled artisan are finite, not infinite, and that the linking of a promoter sequence to a primer to be used in amplifying HIV-1 sequences was known in the art the time of filing.

50. When as here the nucleotide sequence is subject to variability not only in composition but also in length, such speaks not to unexpected results but to routine optimization. It is further noted that the selection of HIV-1 LTR primers in the prior art function in the same manner as that encompassed by the claimed primers. Accordingly, the selection of the exact nucleotide sequence is deemed to be a matter of routine optimization of a finite number of possible choices. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. *In re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; *In re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. *In re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; *In re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. *In re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; *In re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; *In re Irmischer*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More

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particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

51. In view of the above teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Montagnier et al., by using primers directed to LTR region of HIV-1 wherein the primers comprise the nucleotide sequence as set forth by Eberle et al., McDonough et al., and Backus et al., wherein the primer may also include a T7 promoter sequence as disclosed by Stefano et al. As noted above, the primers of the prior art work in the same manner as that of the instant invention- allowing for the amplification of HIV-1 sequences. And in the case of Backus et al., the 3'-terminus of their SEQ ID NO: 2 is identical with that of applicant's SEQ IS NO: 5 and their SEQ ID NO: 4 comprises applicant's SEQ ID NO: 1, therein initiating primer extension at the same positions.

Accordingly, and in view of the great motivation to develop such primers, the well-developed state of the amplification art, said ordinary artisan would have been amply motivated and would have had a most reasonable expectation of success of identifying and making useful HIV-1 primers.

52. Given such explicit motivation and guidance, said ordinary artisan would have had a most reasonable expectation of success.

53. For the above reasons, and in the absence of convincing evidence to the contrary, claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of US Patent 5,413,906 (Eberle et al.), EP 617132 A2

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(McDonough et al.), US Patent 6,001,558 (Backus et al.), US Patent 5,472,840 (Stefano), and applicant's admissions.

Double Patenting

54. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

55. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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56. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

57. Claims 36, 41, 46, and 58-60 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 6 of U.S. Patent No. 6,881,537 in view of US Patent 5,472,840 (Stefano).

58. Claims 1 and 6 of the '537 patent are drawn to a pair of oligonucleotides for the amplification of HIV-1, wherein the primers can comprise 15-26 nucleotides of SEQ ID NO: 1 and 15-26 nucleotides of SEQ ID NO: 5.

59. Neither claim has been found to comprise a limitation of the oligonucleotides/primers comprising a promoter sequence, which is a limitation of independent claims 36, 41, and 46 of the instant application.

60. Stefano, column 30, teaches the ligation of a T7 promoter sequence to an HIV oligonucleotide/primer. Such a showing meets a limitation of independent claims 36, 41, and 46.

61. In view of the admissions of applicant, it would have been obvious to one of ordinary skill in the art at the time of the invention to have developed primers that comprised SEQ ID NO: 1 and 5, or a portion thereof, and wherein one of said primers comprised a promoter sequence such as T7.

Conclusion

62. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

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63. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

64. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

65. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

66. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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67. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

Notice of References Cited	Application/Control No. 11/108,233		Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson		Art Unit 1634	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-4,772,547	09-1988	Heimer et al.	435/5
*	B	US-4,963,532	10-1990	Carter, William A.	514/44R
*	C	US-5,221,610	06-1993	Montagnier et al.	435/7.1
*	D	US-5,413,906	05-1995	Eberle et al.	435/5
*	E	US-5,472,840	12-1995	Stefano, James E.	435/6.11
*	F	US-6,001,558	12-1999	Backus et al.	435/5
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
*	N	EP 617132 A2	09-1994	European Patent	MCDONOUGH et al.	
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.



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BIB DATA SHEET

CONFIRMATION NO. 5814

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
11/108,233	04/18/2005	435	1634	9310-22CT		
RULE						
APPLICANTS Jaap Goudsmit, Amsterdam, NETHERLANDS; Pieter Oudshoorn, Michielsgestel, NETHERLANDS; Suzanne Jurriaans, Monnickendam, NETHERLANDS; Vladimir Vladimirovich Lukashov, Dienen, NETHERLANDS;						
** CONTINUING DATA ***** This application is a CON of 09/463,352 01/21/2000 PAT 6881537 which is a 371 of PCT/EP98/04945 08/05/1998						
** FOREIGN APPLICATIONS ***** EUROPEAN PATENT OFFICE (EPO) 97202455.8 08/08/1997						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/18/2005						
Foreign Priority claimed	☒ Yes ☐ No	☐ Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
35 USC 119(a-d) conditions met	☒ Yes ☐ No	Initials	NETHERLANDS	1	25 9	26 3
Verified and Acknowledged	/BRADLEY L SISSON/ Examiner's Signature					
ADDRESS						
MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627 UNITED STATES						
TITLE						
NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1						
FILING FEE RECEIVED	FEES: Authority has been given in Paper			☐ All Fees		
2500	No. _____ to charge/credit DEPOSIT ACCOUNT			☐ 1.16 Fees (Filing)		
	No. _____ for following:			☐ 1.17 Fees (Processing Ext. of time)		
				☐ 1.18 Fees (Issue)		
				☐ Other _____		
				☐ Credit		

<i>Index of Claims</i> 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
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✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☒ T.D.		☐ R.1.47				
CLAIM		DATE								
Final	Original	10/04/2007	02/06/2008	06/22/2008	09/08/2008	02/23/2009	06/01/2009	09/09/2009	02/21/2010	06/14/2013
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	26	-	-	-	-	-	-	-	-	-
	27	-	-	-	-	-	-	-	-	-
	28	-	-	-	-	-	-	-	-	-
	29	-	-	-	-	-	-	-	-	-
	30	-	-	-	-	-	-	-	-	-
	31	-	-	-	-	-	-	-	-	-
	32	-	-	-	-	-	-	-	-	-
	33	÷	✓	-	-	-	-	-	-	-
	34	÷	✓	=	✓	✓	✓	✓	✓	-
	35	÷	✓	=	✓	✓	✓	-	-	-
	36	÷	✓	=	✓	✓	✓	✓	✓	✓

<i>Index of Claims</i> 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☒ T.D.		☐ R.1.47				
CLAIM		DATE								
Final	Original	10/04/2007	02/06/2008	06/22/2008	09/08/2008	02/23/2009	06/01/2009	09/09/2009	02/21/2010	06/14/2013
	37	÷	✓	-	-	-	-	-	-	-
	38	÷	✓	=	✓	✓	✓	✓	✓	-
	39	÷	✓	-	-	-	-	-	-	-
	40	÷	✓	-	-	-	-	-	-	-
	41	÷	✓	=	✓	✓	✓	✓	✓	✓
	42	÷	✓	=	✓	✓	✓	✓	✓	-
	43	÷	✓	-	-	-	-	-	-	-
	44	÷	✓	-	-	-	-	-	-	-
	45	÷	N	N	N	N	N	-	-	-
	46	÷	✓	=	✓	✓	✓	✓	✓	✓
	47	÷	✓	-	-	-	-	-	-	-
	48	÷	✓	=	✓	✓	✓	✓	✓	-
	49	÷	N	N	N	N	N	N	N	-
	50	÷	N	N	N	N	N	N	N	N
	51	÷	N	N	N	N	N	-	-	-
	52	÷	N	N	N	N	N	N	N	N
	53	÷	N	N	N	N	N	N	N	N
	54	÷	N	-	-	-	-	-	-	-
	55	÷	N	N	N	N	N	N	N	N
	56	÷	N	N	N	N	N	N	N	N
	57					✓	✓	-	-	-
	58									✓
	59									✓
	60									✓

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	52	\$CTCAATAAAGCTTGCGTTGA\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 17:26
L2	39	\$GGGGGOCCTGCTAGAGA\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 18:40
L3	16	\$GGGGGOCCTGCTAGAGA\$ and promoter with primer	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 18:52
S1	6	"6881537"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/27 18:14
S2	11	"7056661"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/27 18:15
S3	49	"6232075"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/27 18:15
S4	1283	"5474796"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:55
S5	12	"5474796" and sisson	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:56
S6	22	"5403707"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:56
S7	43	"5472840"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:56
S8	6	"6881537"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/02/23 20:33
S9	0	WO9907898	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/10/28 15:19
S10	7	"9907898"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/10/28 15:19
S11	1	"9907898"	EPO	OR	OFF	2009/10/28 15:21
S12	19	"20010007747"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/10/29 17:35
S13	22	"5221610"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2011/01/17 14:03

S14	92	(variation variability) same ("HTLV-III" HIV AIDS) same (env LTR) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/07/03 21:58
S15	1	(variation variability) same ("HTLV-III" HIV AIDS) same (env LTR) same primers and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/07/03 21:59
S16	3	koroulis.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2012/07/12 17:10
S17	6070	promoter same (long length) with (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:20
S18	2551	promoter with (long length) with (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:21
S19	822	promoter with (long length) NEAR2 (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:21
S20	327	promoter NEAR4 (long length) NEAR2 (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:22
S21	26	"5122457"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/01/30 08:30
S22	2	"20070048761"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/01/30 17:44
S23	491	(HIV "HIV-1" "HTLV-III" "AIDS virus") same provirus same sequence	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:25
S24	348	(HIV "HIV-1" "HTLV-III" "AIDS virus") same (provirus proviral) same sequence with DNA	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:26
S25	232	(HIV "HIV-1" "HTLV-III" "AIDS virus") with (provirus proviral) same sequence with DNA	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:26
S26	24	(HIV "HIV-1" "HTLV-III" "AIDS virus") with (provirus proviral) same sequence with DNA and @pd<"19970808"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:27
S27	3	koroulis.inv. and array	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 15:13

EAST Search History (Interference)

<This search history is empty>

6/14/2013 7:09:49 PM**C:\Users\bsisson\Documents\EAST\Workspaces\11108233.wsp**

Search Notes 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
435	5, 6, 91.1, 91.2, 91.21, 91.53, 183	6/22/2008	B.L.S.
536	23.1, 24.3, 24.33, 25.3,	6/22/2008	B.L.S.
436	94	6/22/2008	B.L.S.

SEARCH NOTES		
Search Notes	Date	Examiner
Sequence Search (Databases: GenEmbl, N_Geneseq, EST, Published, Issued, Pending)	1/25/2008	B.L.S.
EAST (see transcript for search terms and databases)	2/17/09	B.L.S.
STN, Registry file (SEQ ID NO: 1 & 5)	2/17/09	B.L.S.
Reviewed 11/372577	02/23/09	B.L.S.
EAST (see transcript for databases and search terms)	06/14/2013	B.L.S.

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
435	5, 6, 91.1, 91.2, 91.21, 183	6/22/2008	B.L.S.
536	24.33	6/22/2008	B.L.S.
Sequence Search		1/25/2008	B.L.S.

	/Bradley L Sisson/ Primary Examiner.Art Unit 1634
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Under the Paperwork Reduction Act of 1995 no persons are required to respond to a collection of information unless it displays a valid OMB control number

FEE TRANSMITTAL		Complete if known	
☒ Applicant asserts small entity status. See 37 CFR 1.27. ☐ Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.		Application Number	11/108,233
		Filing Date	April 18, 2005
		First Named Inventor	Jaap Goudsmil
		Examiner Name	Bradley L. Sisson
		Art Unit	1634
TOTAL AMOUNT OF PAYMENT	(\$)	Practitioner Docket No.	9310-22CT

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____
☒ Deposit Account Deposit Account Number: 500220 Deposit Account Name: Myers Bigel
 For the above-identified deposit account, the Director is hereby authorized to (check all that apply):
☐ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, except for the filing fee
☒ Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 ☐ Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

Application Type	FILING FEES			SEARCH FEES			EXAMINATION FEES			Fees Paid (\$)
	U (\$)	S (\$)	M (\$)	U (\$)	S (\$)	M (\$)	U (\$)	S (\$)	M (\$)	
Utility	280	140*	70	600	300	150	720	360	180	
Design	180	90	45	120	60	30	460	230	115	
Plant	180	90	45	380	190	95	580	290	145	
Reissue	280	140	70	600	300	150	2,160	1,080	540	
Provisional	260	130	65	0	0	0	0	0	0	

* The \$140 small entity status filing fee for a utility application is further reduced to \$70 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	Undiscounted Fee (\$)	Small Entity Fee (\$)	Micro Entity Fee (\$)
Each claim over 20 (Including Reissues)	80	40	20
Each independent claim over 3 (Including Reissues)	420	210	105
Multiple dependent claims	780	390	195
Total Claims			
-20 or HP = _____ x _____ = _____			
HP = highest number of total claims paid for, if greater than 20.			
Indep. Claims			
-3 or HP = _____ x _____ = _____			
HP = highest number of independent claims paid for, if greater than 3.			

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$400 (\$200 for small entity) (\$100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fees Paid (\$)
_____ - 100 = _____ / 50 = _____ (round up to a whole number) x _____ = _____				

4. OTHER FEE(S)

	Fees Paid (\$)
Non-English specification, \$130 fee (no small or micro entity discount)	_____
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, \$400 fee (\$200 small or micro entity)	_____
Other (e.g., late filing surcharge): Prioritized examination fee	4000.00

SUBMITTED BY

Signature		Registration No. (Attorney/Agent)	50,211	Telephone	919-854-1400
Name (Print/Type)	Robert A. Schwartzman, Ph.D.			Date	June 3, 2013

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select 4. 06/18/2013 CKHLOK 00000011 500220 11108233

01 FC:1504 300.00 DA
02 FC:1800 130.00 DA
03 FC:1817 4000.00 DA



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MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH NC 27627



Doc Code: TRACK1.GRANT

<i>CORRECTED</i> <i>Decision Granting Request for</i> <i>Prioritized Examination</i> <i>(Track I or After RCE)</i>	Application No.: 11/108,233
The decision mailed June 10, 2013, was issued in error and is hereby <u>VACATED</u>. 1. THE REQUEST FILED <u>6/3/13</u> IS <u>GRANTED</u>. The above-identified application has met the requirements for prioritized examination A. ☐ for an original nonprovisional application (Track I). B. ☒ for an application undergoing continued examination (RCE). 2. The above-identified application will undergo prioritized examination. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs: A. filing a <u>petition for extension of time</u> to extend the time period for filing a reply; B. filing an <u>amendment to amend the application to contain more than four independent claims, more than thirty total claims</u>, or a multiple dependent claim; C. filing a <u>request for continued examination</u>; D. filing a notice of appeal; E. filing a request for suspension of action; F. mailing of a notice of allowance; G. mailing of a final Office action; H. completion of examination as defined in 37 CFR 41.102; or I. abandonment of the application. Telephone inquiries with regard to this decision should be directed to Cheryl Gibson-Baylor at (571)272-3213, Office of Petitions. In his/her absence, calls may be directed to Brian W. Brown, (571)272-5338. Cheryl Gibson-Baylor <u>/Cheryl Gibson-Baylor/</u> [Signature] Petitions Examiner (Title)	

Electronic Acknowledgement Receipt

EFS ID:	15931868
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Robert Andrew Schwartzman/Marthenn Salazar
Filer Authorized By:	Robert Andrew Schwartzman
Attorney Docket Number:	9310-22CT
Receipt Date:	03-JUN-2013
Filing Date:	18-APR-2005
Time Stamp:	15:21:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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Adjustment date: 06/20/2013 SDIBETA1
 06/18/2013 CRHLOK 00000011 500220 11108233
 08 FC-1017 4000.00 CR

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	TrackOne Request	RqstPrioritizedExamination.pdf	144306 7d071112f04e1f50e6b0685d2c42c3f9cb726e0	no	1

Warnings:
Information:



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814
20792 7590 07/11/2013 MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			EXAMINER SISSON, BRADLEY L	
			ART UNIT 1634	PAPER NUMBER
			MAIL DATE 07/11/2013	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<i>Applicant-Initiated Interview Summary</i>	Application No. 11/108,233	Applicant(s) GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson	Art Unit 1634	

All participants (applicant, applicant's representative, PTO personnel):

(1) Bradley L. Sisson, Primary Examiner. (3) _____

(2) Robert Schwartzman, Reg. No. 50,211. (4) _____

Date of Interview: 10 July 2013.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.

If Yes, brief description: _____.

Issues Discussed ☒101 ☐112 ☐102 ☒103 ☐Others

(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: _____.

Identification of prior art discussed: _____.

Substance of Interview

(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Examiner Sisson indicated that a supplemental Office action will be prepared wherein the Rule 132 Declaration of 03 June 2013 will be considered on the record. Examiner Sisson also indicated that the supplemental Office action will be made non-final.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner.
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814
20792 7590 09/16/2013 MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			EXAMINER SISSON, BRADLEY L	
			ART UNIT 1634	PAPER NUMBER
			MAIL DATE 09/16/2013	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action SummaryApplication No.
11/108,233Applicant(s)
GOUDSMIT ET AL.Examiner
Bradley L. SissonArt Unit
1634AIA (First Inventor to File)
Status
No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2013.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 36,41,46,50,52,53,55,56 and 58-60 is/are pending in the application.
5a) Of the above claim(s) 50,52,53,55 and 56 is/are withdrawn from consideration.
- 6) ☐ Claim(s) _____ is/are allowed.
- 7) ☒ Claim(s) 36,41,46 and 58-60 is/are rejected.
- 8) ☐ Claim(s) _____ is/are objected to.
- 9) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 07 October 2011 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

- a) ☒ All b) ☐ Some * c) ☐ None of the:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☒ Certified copies of the priority documents have been received in Application No. 09/463,352.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 4) ☐ Other: _____

DETAILED ACTION

Withdrawal of Finality

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Notice of Pre-AIA or AIA Status

2. The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 June 2013 has been entered.

Election/Restrictions

4. Claims 50, 52, 53, 55, and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on -5 November 2007.

Priority

5. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/463,352, filed on 21 January 2000.

Drawings

6. The drawings were received on 07 October 2011. These drawings are acceptable.

Terminal Disclaimer

7. The terminal disclaimer filed on 26 May 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent Application 11/372,577 has been reviewed and is accepted. The terminal disclaimer has been recorded.
8. The terminal disclaimer filed on 01 May 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent 6,881,537 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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10. Claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter because the claimed invention is directed to a naturally-occurring nucleic acid or fragment thereof, whether isolated or not, that is not patent-eligible pursuant to the Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.* 106 USPQ2d 1972 (US, June 13, 2013).

11. In the particular case, applicant is claiming “oligonucleotide primers for the amplification of a target sequence between two primer binding sites within the LTR region of HIV-1 genome.” As specified by the claim, the two primers are to comprise “a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur...[and] said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur.”

12. Acknowledgement is made that the primer is to comprise nucleotides as depicted in SEQ ID NOs. 1 and 5, and that said sequences are DNA whereas HIV-1 is a retrovirus, that is, it comprises RNA not DNA. The fact that the sequence comprises DNA and not RNA does not render the claimed subject matter patent eligible as it is recognized that, with HIV-1 being a retrovirus, it naturally carries/comprises reverse transcriptase so to naturally produce a proviral sequence, which is DNA. Accordingly, the primer sequences, even if construed as being DNA, is still considered to be a naturally-occurring sequences and, thusly, not patent-eligible subject matter.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of US Patent 5,413,906 (Eberle et al.), EP 617132 A2 (McDonough et al.), US Patent 6,001,558 (Backus et al.), US Patent 5,472,840 (Stefano), and applicant's admissions.

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17. Attention is directed to MPEP 706.02 [R-9]:

III. RELIANCE ON ADMITTED PRIOR ART IN SUPPORT OF REJECTION

A statement by an applicant in the specification or made during prosecution identifying the work of another as “prior art” is an admission which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988). See MPEP § 2129 for discussion on admissions as prior art. Where the admitted prior art anticipates the claim but does not qualify as prior art under any of the paragraphs of 35 U.S.C. 102, the claim may be rejected as being anticipated by the admitted prior art without citing to 35 U.S.C. 102.

18. Attention is directed to MPEP 2129 [R-6], Admissions as Prior Art, which states in part:

I. ADMISSIONS BY APPLICANT CONSTITUTE PRIOR ART

A statement by an applicant >in the specification or made< during prosecution identifying the work of another as “prior art” is an admission **>which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988).

19. Attention is also directed to *Ex parte Shirley*, (BPAI, 2009) Appeal No. 2009002352, which, at pages 21 and 26, states:

The Specification’s omission of the term “prior art” and inclusion of the prior-art disclaimer may initially appear to indicate that Appellants do not consider the single-step soft bake process to constitute prior art. To place these latter, contraindicative factors into the proper context though, we note that patent-application drafters regularly endeavor to avoid the indiscriminate or imprudent use of the descriptive label, “prior art.” See *Riverwood Intern. Corp. v. R.A. Jones & Co., Inc.*, 324 F.3d 1346, 1354 (Fed. Cir. 2003) (citing *In re Fout*, 675 F.2d 297, 300 (CCPA 1982)) for the proposition that “section 102 is not the only source of ... prior art. Valid prior art may be created by the admissions of the parties”; *In re Nomiya*, 509 F.2d 566, 571 (CCPA 1975) (holding that an Applicant’s labeling of certain figures as “prior art,” *ipsissimis verbis*, constituted an admission that the pictured subject matter was prior art relative to Applicant’s invention); MPEP § 21294 (instructing that “the examiner must determine whether the subject matter identified as ‘prior art’ is applicant’s own work, or the work of another. In the absence of

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another credible explanation, examiners should treat such subject matter as the work of another”).

The Specification's omission of the term “prior art” and inclusion of the boilerplate prior-art disclaimer do not change our conclusion. In view of the record as a whole, these factors are ineffective in shielding Appellants from having their prior-art admissions treated as such.

20. Attention is directed to MPEP 904.01.

The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co., Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992). In added support of this position, attention is directed to MPEP 2111 [R-9], where, citing *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969), is stated:

The court explained that “reading a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim, is a quite different thing from ‘reading limitations of the specification into a claim,’ to thereby narrow the scope of the claim by implicitly adding disclosed limitations which have no express basis in the claim.” The court found that applicant was advocating the latter, i.e., the impermissible importation of subject matter from the specification into the claim.

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Additionally, attention is directed to MPEP 2111.01 [R-9], wherein is stated:

II. IT IS IMPROPER TO IMPORT CLAIM LIMITATIONS FROM THE SPECIFICATION

“Though understanding the claim language may be aided by explanations contained in the written description, it is important not to import into a claim limitations that are not part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment.” *Superguide Corp. v. DirecTV Enterprises, Inc.*, 358 F.3d 870, 875, 69 USPQ2d 1865, 1868 (Fed. Cir. 2004).

21. Claims 36, 41, and 46 are independent. Claim 36 is deemed representative and, for convenience, is reproduced below.

36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer is ~~a maximum of 50 nucleotides in length and comprises (1) a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15-40-26 nucleotides in length and comprising at least 15-40 sequential nucleotides of the nucleotide sequence of:~~

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA; ~~and~~

~~(2) a promoter operably linked to said first oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and~~

wherein said second primer comprises a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

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22. For purposes of examination, the claimed "pair of oligonucleotide primers" has been construed as encompassing the required primer pair, but that the individual primer pair can have additional nucleotide sequences present as a result of the use of the expression "comprising."

While the first and second primers are to "comprise" a first and second oligonucleotide, there is nothing in the claim that precludes the individual primers from comprising additional nucleotide sequences.

23. Upon review of the instant disclosure it is noted that there is no part of the disclosure that is labeled as being directed to "Prior Art," or that any of the cited documents constitute "prior art." However, the instant disclosure has been found to specifically identify documents that were published prior to the effective filing date of the subject application. Such documents and applicant's characterization as to what they disclose are considered to be admissions as to prior art. Additionally, a review of the disclosure has also found statements by applicant as to what was known in the art at the time of the invention. Such statements are also considered to be admissions of prior art.

24. Applicant, at page 2 of the disclosure admits:

Some regions are more prone to sequence variation than others. Especially in the *env* domain sequence variation can be as high as 30% between members of the different subtypes. Ideally, primer selection should be based on knowledge of interstrain variability in candidate primer sequences and the consequences of mismatching at primer sites. McCutchan et al, J.AIDS, 4, 1241-1250, 1991, used PCR to make a genetic comparison of different HIV-1 isolates. Using anchored PCR (varying sense primers were used with a constant antisense primer, primers were chosen from relatively conserved regions in gag, env and LTR)

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25. Upon review of the above statement, it is not clear if the characterization of the percent variability of the *env* gene is an admission of prior art or whether it is information obtained by applicant. In answering this question, it is noted that US Patent 4,772,547 (Heimer et al.), which was published nearly 9 years prior to the effective filing date of the subject application, teaches in column 5, third paragraph, that the variability of the *env* gen can be as much as 20 %.

Additionally, US Patent 4,963,532 (Carter), which issued 16 October 1990, nearly 7 years prior to the effective filing date of the subject application, states in column 1, lines 32-34: "The most variable region of the HIV genome is the envelope (*env*) gene..." In view of the state of the art at the time of filing, these statements are deemed to be admissions of prior art.

26. Applicant, at page 2, last paragraph, bridging to page 3, of the disclosure states:

Research aimed at identifying suitable primer sets for the reliable amplification of HIV-1 derived nucleic acid sequences has been ongoing for the past years. Engelbrecht et al., *J. Virol. Meth.*, 55, 391-400, 1995, describe a study aimed at the development of a specific and sensitive PCR protocol using *env*, *gag* and LTR primer pairs to detect subtypes present in the Western Cape, South Africa. Twenty four strains of which it was known that they belonged to subtypes B, C and D were analyzed.

27. Applicant, at page 3, last paragraph, admits:

Various techniques for amplifying nucleic acid are known in the art.

28. Montagnier et al., column 1, states;

Acquired immune deficiency syndrome (AIDS) is a condition which is now of major importance in North America, Europe, and Central Africa. The causal agent of AIDS is believed to be a retrovirus. Recent estimates suggest that approximately 1 million Americans may have been exposed to the AIDS virus. The individuals affected show severe immunosuppression, which may be followed by the onset of fatal diseases.

It is now universally recognized that viruses previously denominated lymphadenopathy associated virus (LAV), immune deficiency associated virus (IDAV1 and IDAV2),

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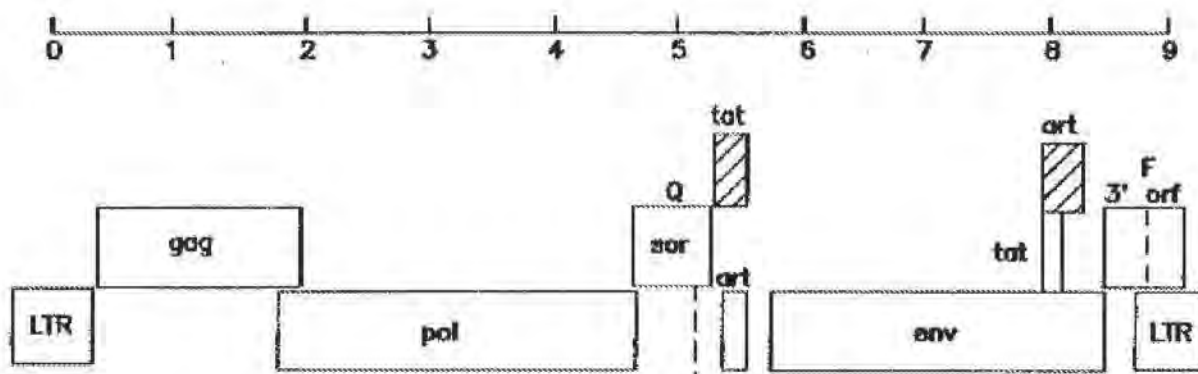
human T-lymphotropic virus type III (HTLV-III), and AIDS related virus (ARV) are all variants of the same retrovirus. See, *e.g.*, Nature, 313:636-637 (1985).

A subcommittee empowered by the International Committee on the Taxonomy of Viruses recently proposed that the AIDS retroviruses be officially designated as the "Human Immunodeficiency Viruses," to be known in abbreviated form as "HIV."

Montagnier et al., column 2, states:

Moreover, there are compelling epidemiological considerations that make early detection of infection by the AIDS virus essential. Thus, for example, infection of an individual with the AIDS virus may be suspected because of the clinical symptoms manifested by the individual, but the infection may be in a very late stage before these symptoms are observed. Meanwhile, transmission of the disease may have taken place.

29. The structure/organization of the nucleotide sequence of HIV-1 as well as the nucleotide sequence of same are known in the art at the time of filing. Montagnier et al., in Figure 1, presents a graphic showing the relative size of the genome in kilobases as well as its organization.



As is readily apparent from the cropped image of FIG. 1, *supra*, the genetic organization of HIV-1 comprises a Long Terminal Repeat (LTR) region on both ends of the genome, and that the relative size of the LTR regions constitute but a very small segment of the genome.

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30. While Montagnier et al., do teach of serologic testing and the polypeptides and antibodies that could be used in such methodologies, they unequivocally consider polynucleotides, such as primers, to also be part of their invention. In support of this position, attention is directed to column 18 where Montagnier et al., refer explicitly to “polynucleotides of the invention.”

31. Montagnier et al., provide motivation for the selection and use of primers for the detection of HIV-1 infected individuals were at column 18, bridging to column 19, Montagnier et al., teach that a PCR assay can be conducted in “less than three days” and can be used to detect HIV provirus (the cDNA copy of the RNA of the HIV-1 genome that has integrated into the chromosomes of the host (human) cell). In comparison, a serologic “procedure can take up to three to four weeks and lacks sensitivity in that viruses cannot be consistently isolated from persons with documented infections.” Such explicit statements by Montagnier et al., clearly provides motivation to one of skill in the art to develop primers that can be used to detect HIV-1 infection in an individual not only in a considerably faster method, but also in a more sensitive approach in that the virus can be detected before the patient expresses virus or produces any antibodies against the virus.

32. Montagnier et al., column 19, bridging to column 20, teach of the potential that any given individual may have been exposed to HIV-1 with genetic variations, and that detection of the particular variant(s) of HIV-1 that an individual has been exposed to “is preferably carried out” using primers and probes “derived from highly conserved regions of the viral genome, such as the LTR...”

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33. As set forth above, Montagnier et al., clearly recognize the need, if not urgency, in developing a faster and more sensitive assay, that PCR would provide such a detection mechanism, and then directs one of skilled in the art to not only the specific region of the HIV-1 genome, but also further directs one to develop primers that correspond to “highly conserved regions” of the LTR.

34. Applicant, at page 8 of the disclosure, teaches that the primers/oligonucleotides are “substantially complementary to a sequence of the LTR region of a nucleic acid sequence of a HIV genome.” Nucleic acids corresponding to SEQ ID NO: 1 and 5 are specifically identified. This is the very region that Montagnier et al., explicitly directs one of skill in the art to go to and select primers

35. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007):

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

36. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes “background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR* at 1396. In demonstration of the “specialized understanding of one of ordinary skill in the art, and

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the common understanding of the layman,” it is noted that STN Registry No. 11793-79-3 discloses the nucleotide sequence of the LTR of HIV-1.

37. Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

38. In the present case, the prior art clearly establishes that there were design pressures and market needs for primers that would allow for the detection of HIV-1 genome via PCR. The prior art also clearly establishes that the structure and nucleotide sequence of the HIV-1 genome was known- including the propensity of numerous variants to develop. The prior art also explicitly directs one of skill in the art to select primers not only from the LTR region of HIV-1, but also from those regions that are “highly conserved.” With the prior art teaching one to focus on such a small area, “there are a finite number of identified, predictable solutions.”

39. Montagnier et al., do teach the development of primers from LTR region of HIV-1, and that these primers are to be used in polymerase chain reaction (PCR), the very use that applicant has disclosed. Accordingly, the selection of size of primer size (15-26 nucleotides for the “first oligonucleotide” component of the first primer, and 10-26 nucleotides for the “second oligonucleotide” of the “second primer” (claims 36, 41, 46) and 15-26 nucleotides for the “second oligonucleotide” of the “second primer” (claims 58-60) is deemed to be a matter of obvious design choice for as the instant application does not present any showing that the claimed primers have any unexpected property or yield any unexpected result when used.

40. Attention is directed to MPEP 2112 [R-3]:

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The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references).

In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." *Id.*

MPEP 2112 II:

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.")

41. Montagnier et al., has not been found to disclose coupling a primer to a promoter nucleotide sequence (limitation of independent claims 36, 41, 46).

42. Eberle et al., column 14, disclose primers directed to LTR of HIV-1. As can be seen therein, the disclosed primer (SEQ ID NO. 1) is 18 nucleotides in length. Also, the primer of Eberle et al., shares the nucleotides GGGCGCCA with that of the instant SEQ ID NO. 1.

43. Eberle et al., has not been found to disclose using additional sequences of LTR, or the inclusion of a T7 promoter sequence coupled to the primer.

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44. McDonough discloses in their SEQ ID NO. 50 the complete nucleotide sequence of applicant's SEQ ID NO. 1. As can be seen, SEQ ID NO. 50 contains an additional 4 nucleotides at the 5' terminus and an additional nucleotide at the 3' terminus. By comparison, applicant's first and second primers have been amended such that they no longer have any upper limit. In support of this position, it is noted that claim 36 recites that the "first primer comprises a first oligonucleotide" and that the second primer "comprises a second oligonucleotide." There is no restriction as to the number of additional "oligonucleotides" (or any other component) that each primer can "comprise" so long as it is still functional. Additionally, it is noted that the "first oligonucleotide" of the "first primer" can be 26 nucleotides in length and have but 15 nucleotides corresponding to HIV-1 LTR sequence. Given such, the remaining 11 nucleotides are undefined. Recognizing that each of these undefined 11 positions can be occupied by any one of the four common dNTPs, there are 4^{11} , or 4,194,304 different possible sequences for just these 11 positions when present in a continuous series. In the case of the "second primer" whose oligonucleotide can also be 26 nucleotides in length yet only have 10 sequential nucleotides of the SEQ ID NO: 5, there are some 4^{16} , or 4,294,967,296 different primers where all 16 of the undefined positions occur consecutively.

45. Backus et al., disclose an HIV-1 LTR primer, their SEQ ID NO: 2, which is some 30 nucleotides in length and comprises all of applicant's SEQ ID NO: 5. Additionally, SEQ ID NO: 4 of Backus et al., which comprises some 23 nucleotides, comprises the full length SEQ ID NO: 1 claimed instantly, which by way of comparison, is 18 nucleotides in length. It is further noted that the 3' nucleotide sequence of the prior art SEQ ID NO: 4 is the same as the 3' sequence of applicant's SEQ ID NO: 1. Given such explicit teachings, it is clearly evident that the prior art

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not only fairly points the skilled artisan to the conserved regions of the LTR of HIV-1, but also specifically identifies the same nucleotide sequence for use as a primer.

46. Backus et al., have not been found to teach incorporating a promoter into the primer.

47. Stefano, column 30, teaches the ligation of a T7 promoter sequence to an HIV oligonucleotide/primer. Such a showing meets a limitation of independent claims 36, 41, and 46.

48. Independent claims 36, 41, and 46 require the primers to further comprise a promoter region, which in dependent claims 38, 42, and 48 is limited to "a T3, T7, or SP6 promoter."

49. Applicant, at page 4 of the disclosure, admits:

Another technique for the amplification of nucleic acid is the so-called transcription based amplification system (TAS). The TAS method is described in International Patent Appl. no. WO 88/10315. Transcription based amplification techniques usually comprise treating target nucleic acid with two oligonucleotides one of which comprises a promoter sequence, to generate a template including a functional promoter. Multiple copies of RNA are transcribed from said template and can serve as a basis for further amplification.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are described in EP 408295. EP 408295 is primarily concerned with a two-enzyme transcription based amplification method. Transcription based amplification methods, such as the NASBA method as described in EP 329822, are usually employed with a set of oligonucleotides, one of which is provided with a promoter sequence that is recognized by a DNA dependent RNA polymerase such as, for example, T7 polymerase. Several modifications of transcription based techniques are known in the art.

In contrast to RT-PCR, NASBA, which is based on RNA transcription by T7 RNA polymerase (Kievits et al., 1991; Compton, 1991), does not need differentiation between RNA- and DNA- derived amplification products since it uses RNA as its principal target. NASBA enables specific amplification of RNA targets even in a background of DNA.

An isothermal continuous transcription based amplification method is the so-called NASBA process ("NASBA") as described in European Patent no. EP 329822. NASBA includes the use of T7 RNA polymerase to transcribe multiple copies of RNA from a template including a T7 promoter. Other transcription based amplification techniques are

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described in EP 408295... One or more "promoter-primers" (oligonucleotides provided with a promoter sequence) may be used in transcription based amplification techniques, optionally combined with the use of one or more oligonucleotides that are not provided with a promoter sequence. For RNA amplification, a transcription based amplification technique, is a preferred technology.

In each of the above-reproduced paragraphs, applicant has provided a summary of the disclosures of the various documents. Such statements, while not labeled as "prior art," are considered to be admissions of prior art.

50. In view of the admitted state of the art where primers comprising a promoter region, such as T7, are used in transcription-based amplification methods, and that the inclusion of the T7 promoter in such primers was known in the art, and that NASBA does not need differentiation between RNA- and DNA-derived amplification products, one of ordinary skill in the art at the time of the invention would have been motivated to have included just such a promoter on the HIV-1 primers as such would have allowed for the amplification of HIV-1 sequences, be they RNA as found in the viral particles, or DNA, as is found when HIV-1 has integrated into a hosts genome (proviral sequence).

51. As set forth above, the prior art clearly provides motivation for one of skill in the art to produce useful primers that would allow for the amplification of HIV-1 sequences, and directs the public to select primers from the LTR region of HIV-1. And as seen above, Backus et al., actually discloses primers that comprise the nucleotide sequence of applicants' SEQ ID NO: 1 and 5. The rejection has set forth that the number of choices confronting the skilled artisan are finite, not infinite, and that the linking of a promoter sequence to a primer to be used in amplifying HIV-1 sequences was known in the art the time of filing.

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52. When as here the nucleotide sequence is subject to variability not only in composition but also in length, such speaks not to unexpected results but to routine optimization. It is further noted that the selection of HIV-1 LTR primers in the prior art function in the same manner as that encompassed by the claimed primers. Accordingly, the selection of the exact nucleotide sequence is deemed to be a matter of routine optimization of a finite number of possible choices. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. *In re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; *In re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. *In re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; *In re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. *In re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; *In re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; *In re Irmscher*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

53. In view of the above teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Montagnier et al., by using primers directed to LTR region of HIV-1 wherein the primers comprise the nucleotide sequence as set forth by Eberle et al., McDonough et al., and Backus et al., wherein the primer

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may also include a T7 promoter sequence as disclosed by Stefano et al. As noted above, the primers of the prior art work in the same manner as that of the instant invention- allowing for the amplification of HIV-1 sequences. And in the case of Backus et al., the 3'-terminus of their SEQ ID NO: 2 is identical with that of applicant's SEQ IS NO: 5 and their SEQ ID NO: 4 comprises applicant's SEQ ID NO: 1, therein initiating primer extension at the same positions.

Accordingly, and in view of the great motivation to develop such primers, the well-developed state of the amplification art, said ordinary artisan would have been amply motivated and would have had a most reasonable expectation of success of identifying and making useful HIV-1 primers.

54. Given such explicit motivation and guidance, said ordinary artisan would have had a most reasonable expectation of success.

55. For the above reasons, and in the absence of convincing evidence to the contrary, claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of US Patent 5,413,906 (Eberle et al.), EP 617132 A2 (McDonough et al.), US Patent 6,001,558 (Backus et al.), US Patent 5,472,840 (Stefano), and applicant's admissions.

Response to argument

56. The declaration under 37 CFR 1.132 filed 03 June 2013 is insufficient to overcome the rejection of claims 36, 41, 46, and 58-60 under 35 U.S.C. 103(a) based upon US Patent 5,221,610 (Montagnier et al.) in view of US Patent 5,413,906 (Eberle et al.), EP 617132 A2 (McDonough et al.), US Patent 6,001,558 (Backus et al.), US Patent 5,472,840 (Stefano), and

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applicant's admissions as set forth in the last Office action because: The showing is not commensurate in scope.

57. As set forth in the declaration, declarant presents evidence that under specific conditions, one embodiment of the claimed primers has been found to achieve better results over that of the prior art. Such a showing does not indicate that the prior art primers can function equally well, albeit under different (optimized) conditions. Further, there is no requirement that the primers ever be used in an amplification reaction as the claims are drawn to a product, not a method of using. Further still, the showing does not address the aspect of scope in that the claims fairly encompass primer pair where the primers, be it individually or in combination, comprise additional (naturally-occurring) nucleotide sequences, which can include the entire sequence of the prior-art primers as well as additional nucleotides, be they from HIV or a non-HIV source.

58. For the above reasons and in the absence of convincing evidence to the contrary, claims 36, 41, 46, and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,221,610 (Montagnier et al.) in view of US Patent 5,413,906 (Eberle et al.), EP 617132 A2 (McDonough et al.), US Patent 6,001,558 (Backus et al.), US Patent 5,472,840 (Stefano), and applicant's admissions.

Double Patenting

59. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

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is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

60. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

61. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

62. Claims 36, 41, 46, and 58-60 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 6 of U.S. Patent No. 6,881,537 in view of US Patent 5,472,840 (Stefano).

63. Claims 1 and 6 of the '537 patent are drawn to a pair of oligonucleotides for the amplification of HIV-1, wherein the primers can comprise 15-26 nucleotides of SEQ ID NO: 1 and 15-26 nucleotides of SEQ ID NO: 5.

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64. Neither claim has been found to comprise a limitation of the oligonucleotides/primers comprising a promoter sequence, which is a limitation of independent claims 36, 41, and 46 of the instant application.

65. Stefano, column 30, teaches the ligation of a T7 promoter sequence to an HIV oligonucleotide/primer. Such a showing meets a limitation of independent claims 36, 41, and 46.

66. In view of the admissions of applicant, it would have been obvious to one of ordinary skill in the art at the time of the invention to have developed primers that comprised SEQ ID NO: 1 and 5, or a portion thereof, and wherein one of said primers comprised a promoter sequence such as T7.

Conclusion

67. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

68. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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69. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

70. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

71. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

Notice of References Cited	Application/Control No. 11/108,233		Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson		Art Unit 1634	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,221,610	06-1993	Montagnier et al.	435/7.1
*	B	US-5,413,906	05-1995	Eberle et al.	435/5
*	C	US-5,472,840	12-1995	Stefano, James E.	435/6.11
*	D	US-6,001,558	12-1999	Backus et al.	435/5
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
*	N	EP 617132 A2	09-1994	European Patent	MCDONOUGH et al.	
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
435	5, 6, 91.1, 91.2, 91.21, 91.53, 183	6/22/2008	B.L.S.
536	23.1, 24.3, 24.33, 25.3,	6/22/2008	B.L.S.
436	94	6/22/2008	B.L.S.

SEARCH NOTES		
Search Notes	Date	Examiner
Sequence Search (Databases: GenEmbl, N_Geneseq, EST, Published, Issued, Pending)	1/25/2008	B.L.S.
EAST (see transcript for search terms and databases)	2/17/09	B.L.S.
STN, Registry file (SEQ ID NO: 1 & 5)	2/17/09	B.L.S.
Reviewed 11/372577	02/23/09	B.L.S.
EAST (see transcript for databases and search terms)	06/14/2013	B.L.S.

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
435	5, 6, 91.1, 91.2, 91.21, 183	6/22/2008	B.L.S.
536	24.33	6/22/2008	B.L.S.
Sequence Search		1/25/2008	B.L.S.

	/Bradley L Sisson/ Primary Examiner.Art Unit 1634
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814
20792 7590 11/21/2013 MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			EXAMINER SISSON, BRADLEY L	
			ART UNIT 1634	PAPER NUMBER
			MAIL DATE 11/21/2013	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<i>Applicant-Initiated Interview Summary</i>	Application No. 11/108,233	Applicant(s) GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson	Art Unit 1634	

All participants (applicant, applicant's representative, PTO personnel):

- (1) Bradley L. Sisson, Primary Examiner. (3) Robert Schwartzman, Reg. No. 50,211.
 (2) Jean Witz, QAS. (4) Continued under "Substance of Interview".

Date of Interview: 19 November 2013.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
 If Yes, brief description: _____.

Issues Discussed ☒101 ☐112 ☐102 ☒103 ☐Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: 36, 41, 46, and 58-60.

Identification of prior art discussed: Bell and Ratner, Aids Res Human Retroviruses 5:87-95 (1989); US Patent 5,221,610 (Montagnier); US Patent 5,472,840 (Stefano); EP 617132 A2 (McDonough et al.); and US Patent 6,001,558 (Backus).

Substance of Interview

(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

See Continuation Sheet.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/Bradley L. Sisson/
 Primary Examiner, Art Unit 1634

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135, (35 U.S.C. 132).

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner.
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments:

Participants, continued:

5) Alice Bonnen, Reg. No. 57,154

6) Elizabeth Worley, Reg. No. 38,298.

Examiner Sisson indicated that, upon discussion with QAS Witz, it is agreed that the rejection of claims 36, 41, 46, and 58-60 under 35 USC 101 would be withdrawn.

The rejection of claims under 35 USC 103(a) was discussed. Mr. Schwartzman directed attention to the Rule 1.312 declaration of Ali Laayoun, Ph.D., filed 03 June 2013. In response to inquiry by QAS Witz, Mr. Schwartzman indicated that the Bell and Ratner reference (Aids Res Human Retroviruses 5:87-95 (1989)) had not been used in a rejection by the US Patent Office, but it had been cited by a foreign office.

Mr. Schwartzman directed attention to page 13 and how the various primer sequences correspond to one another. And attention was also directed to page 12, Table 1, and how the primers based on 10 nucleotide addition to either the 5' or 3' terminus of the core sequence gave superior results over the closely-related primer disclosed in Bell and Ratner.

Examiner Sisson and QAS Witz indicated agreement that such a showing may well be persuasive towards the withdrawal of the rejection.

Mr. Schwartzman indicated that a response to the non-final Office action of 16 September 2013 would be filed shortly.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.	Confirmation No. 5814
Application No.: 11/108,233	Group Art Unit: 1634
Filed: April 18, 2005	Examiner: Bradley L. Sisson
Title: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1	

November 25, 2013

Mail Stop Amendment
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE TO SEPTEMBER 16, 2013 OFFICE ACTION

Sir:

This paper is responsive to the Office Action mailed September 16, 2013 regarding the above-referenced patent application. Please enter the following amendments and reconsider the rejections of the claims for at least the reasons presented in the following remarks.

If any extension of time for the accompanying response or submission is required, Applicants requests that this be considered a petition therefor. The Commissioner is hereby authorized to charge any additional fee, which may be required, or credit any refund, to our Deposit Account No. 50-0220.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 6 of this paper.

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-35. (canceled)

36. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer consists essentially of ~~comprises~~ a first oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15-26 nucleotides in length and comprising at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA;

said first oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer consists essentially of ~~comprises~~ a second oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

37-40. (canceled)

41. (currently amended) A primer set for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said set consisting of a first primer and a second primer,

wherein said first primer consists essentially of ~~comprises~~ a first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15-26 nucleotides in length and comprising at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA;

said first hybridizing oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer consists essentially of ~~comprises~~ a second hybridizing oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

42-45. (canceled)

46. (currently amended) A pair of oligonucleotide primers for the amplification of a target sequence between two primer binding sites located within the LTR region of the HIV-1 genome, said pair consisting of a first primer and a second primer,

wherein said first primer consists essentially of ~~comprises~~ a first hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region at a first primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 15-26 nucleotides in length, wherein said first hybridizing oligonucleotide comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:1: G GGC GCC ACT GCT AGA GA;

said hybridizing oligonucleotide being operably linked to a T3, T7, or SP6 promoter; and

wherein said second primer consists essentially of ~~comprises~~ a second hybridizing oligonucleotide that is fully complementary to a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site and binds thereto under conditions whereby nucleic acid amplification can occur, said oligonucleotide being 10-26 nucleotides in length, wherein said second hybridizing oligonucleotide comprises at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA

wherein said primers amplify the target sequence between the two primer binding sites located within the LTR region of the HIV-1 genome when contacted with HIV-1 nucleic acid under conditions whereby nucleic acid amplification can occur.

47-57. (canceled)

58. (previously presented) The pair of oligonucleotide primers of claim 36, wherein said second oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

59. (previously presented) The primer set of claim 41, wherein said second hybridizing oligonucleotide that is fully complementary to a sequence of the LTR region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

60. (previously presented) The pair of oligonucleotide primers of claim 46, wherein said second hybridizing oligonucleotide that is fully complementary to a sequence of the LTR

region is 15-26 nucleotides in length and comprises at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO:5: CTC AAT AAA GCT TGC CTT GA.

61. (canceled)

REMARKS

Upon entry of the foregoing amendment, claims 36, 41, 46, and 58-60 are pending in the application, with 36, 41, and 46 being the independent claims. Claims 50, 52, 53, 55, and 56 have been canceled without prejudice or disclaimer. Claims 36, 41, and 46 have been amended to claim the invention with more particularity. Support for the amendments is found in the claims as originally filed and in the specification at least at page 6, line 35 to page 7, line 16. No new matter has been added.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Interview Summary

Applicants appreciate the courtesies that were extended by Examiner Sisson and Quality Assurance Specialist Witz to Robert Schwartzman, Alice Bonnen, and Elizabeth Worley during the telephonic interview on November 19, 2013. Applicants concur that the Interview Summary mailed November 21, 2013 accurately reflects the substance of the interview.

Rejections Under 35 U.S.C. § 112

Claims 36, 41, 46, and 58-60 have been rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. (Office Action, page 4). Applicants respectfully traverse this rejection.

The Examiner states that the claimed invention is directed to a naturally-occurring nucleic acid or fragment thereof which is not patent-eligible pursuant to the Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.* 106 USPQ2d 1972 (June 13, 2013). (Office Action, page 4).

Applicants respectfully disagree. Applicants point out that the first primer consists of an oligonucleotide complementary to the LTR region of HIV-1 which is operably linked to a T3, T7, or SP6 promoter. As HIV-1 and T3, T7, or SP6 are different organisms, the HIV-1 oligonucleotide is not found in nature linked to a T3, T7, or SP6 promoter. Thus, the first primer clearly is not a naturally-occurring nucleic acid and is patent-eligible under *Myriad*.

Additionally, while the HIV-1 genome is a naturally occurring nucleic acid, the claimed oligonucleotide primers are not segments that are found together in nature. Thus, the pair of primers clearly is not a naturally-occurring nucleic acid and is patent-eligible under *Myriad*.

Applicants respectfully request that the rejection of claims 36, 41, 46, and 58-60 under 35 U.S.C. § 101 be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 36, 41, 46, and 58-60 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Montagnier *et al.* (U.S. Patent No. 5,221,610, hereafter “Montagnier”) in view of Eberle *et al.* (U.S. Patent No. 5,413,906, hereafter “Eberle”), McDonough *et al.* (EP Patent No. 617132, hereafter “McDonough”), Backus *et al.* (U.S. Patent No. 6,001,558, hereafter “Backus”), Stefano *et al.* (U.S. Patent No. 5,472,840, hereafter “Stefano”), and Applicants’ alleged admissions. (Office Action, page 5). Applicants respectfully traverse this rejection.

Applicants’ response to the citation of Montagnier and Applicants’ alleged admissions was set forth in detail in the response filed June 3, 2013 and is reiterated here.

The Examiner has added Eberle, McDonough, and Backus to the rejection, alleging that these references identify the same nucleotide sequences for use as a primer as is presently claimed. (Office Action, pages 15-17). Applicants respectfully disagree. None of these references disclose the presently claimed primer pair. None of the references disclose a primer linked to a promoter as required for the first primer of the present claims. None of the references disclose a primer that is encompassed by the second primer of the present claims. Thus, while these references may direct one of ordinary skill in the art generally to certain regions of the LTR, the references, either alone or together, do not teach or suggest the specific primer pair claimed here. As discussed below, Applicants have provided declaratory evidence showing that even small changes in the primer location have tremendous effects on the ability of the primers to amplify HIV-1 sequences. Thus, general teachings directing one to regions of the LTR are not sufficient to render the present claims obvious.

Applicants submitted in the response filed June 3, 2013 a Declaration of Ali Laayoun, Ph.D. Pursuant to 37 C.F.R. § 1.132 (hereinafter, “the Laayoun Declaration”). As discussed in the interview of November 19, 2013, the Laayoun Declaration supports Applicant’s assertions

regarding the non-obviousness of the claimed primer pairs by demonstrating the superiority of the claimed primer pairs in terms of amplification efficiency and detection sensitivity in nucleic acid amplification assays compared to other primers targeting the HIV LTR.

In response to the Laayoun Declaration, the Examiner stated that the showing is not commensurate in scope with the claims as the Declaration presents evidence that under specific conditions, one embodiment of the claimed primers has been found to achieve better results over that of the prior art. (Office Action, page 21). Applicants respectfully disagree and submit that the Laayoun Declaration provides broad evidence of unexpected results over the full scope of the claims. Figure 13 on page 13 of the Laayoun Declaration depicts all of the primers that were tested in the disclosed experiments. These include three different primers corresponding to the first primer of the claims (primers 1A-1C) and seven different primers corresponding to the second primer of the claims (SEQ ID NO:5 and 5A-5F). For both sets of primers, the variants tested include extensions at both the 5' and 3' ends of the primers. Additionally, as shown in Tables 1 and 2 on page 12 of the Laayoun Declaration, different primer lengths were tested, including lengths of 18 and 26 nucleotides for the first primer and lengths of 18, 20, and 22 nucleotides for the second primer. Every one of the primers tested was shown to provide superior amplification and detection compared to the prior art primers. Moreover, primers having the sequence of SEQ ID NOS: 1 and 5 were tested in three different amplification assays, NASBA, PCR, and RT-PCR. The primers were shown to provide superior amplification and detection in each of the three assays compared to the prior art primers, demonstrating that the results are not limited to a single set of conditions. Thus, the data in the Laayoun Declaration supports the finding of unexpected results over the full scope of the claims.

The significant superiority of the claimed primers over the prior art primers as demonstrated in a direct comparison is more than sufficient to outweigh any alleged a *prima facie* case of obviousness. Accordingly, Applicants respectfully submit that the claimed primers were not obvious as of the effective filing date of the present application.

Applicants respectfully request that the rejection of claims 36, 41, 46, and 58-60 under 35 U.S.C. § 103(a) be withdrawn.

Double Patenting

The Examiner has rejected claims 36, 41, 46, and 58-60 for obviousness-type double patenting over claims 1 and 6 of U.S. Patent No. 6,881,537 in view of U.S. Patent No. 5,472,840. (Office Action, page 22).

Applicants respectfully point out that a terminal disclaimer over U.S. Patent No. 6,881,537 was filed May 1, 2008. Thus, the rejection is moot.

Applicants respectfully request that the rejection of claims 36, 41, 46, and 58-60 for obviousness-type double patenting be withdrawn.

CONCLUSION

Accordingly, Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any small matters outstanding of resolution, he is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

No fee other than those accompanying this response is believed to be due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



Robert A. Schwartzman, Ph.D.
Registration No. 50,211

Customer Number 20792

Myers Bigel Sibley & Sajovec, P.A.
P.O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on November 25, 2013.

Signature: _____

Marthenn Salazar

Electronic Acknowledgement Receipt

EFS ID:	17493266
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Robert Andrew Schwartzman/Marthenn Salazar
Filer Authorized By:	Robert Andrew Schwartzman
Attorney Docket Number:	9310-22CT
Receipt Date:	25-NOV-2013
Filing Date:	18-APR-2005
Time Stamp:	14:18:57
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		Amendment.pdf	323034 943051e8157f94c212cf53e072afa2170b58569	yes	9

	Multipart Description/PDF files in .zip description		
	Document Description	Start	End
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Claims	2	5
	Applicant Arguments/Remarks Made in an Amendment	6	9
Warnings:			
Information:			
Total Files Size (in bytes):		323034	
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.			

DO NOT ENTER: /BLS/

Attorney Docket No. 9310-22CT

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.

Confirmation No.: 5814

Application Serial No.: 11/108,233

Examiner: B. Sisson

Filing Date: April 18, 2005

Group Art Unit: 1634

For: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN
THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1

May 26, 2009

Mail Stop Amendment

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

RESPONSE

Sir:

This is responsive to the February 26, 2009 Office Action issued regarding the above-referenced patent application. A Terminal Disclaimer is included herewith. Please enter the following amendments and consider the following remarks.

Substitute form 1449A/PTO

Complete if Known

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	1	Attorney Docket Number	9310-22CT
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U.S. PATENTS AND PATENT PUBLICATIONS

Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code (if known)		
	1.	5,221,610		Montagnier et al.	06-1993
	2.	5,306,631		Harrison et al.	04-1994
	3.	5,474,796		Brennan	12-1995
	4.	5,576,176		Adams et al.	11-1996
	5.	5,712,385		McDonough et al.	01-1998
	6.	5,770,428		Boris-Lawrie	06-1998
	7.	6,001,558		Backus et al.	12-1999
	8.	6,025,124		Adams et al.	02-2000

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation
		Office	Number	Kind Code (if known)			
	9.	EP	0617132	A2	McDonough et al.	08-1993	

OTHER NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T
	10.	De Baar et al., <i>Journal of Clinical Microbiology</i> , vol. 37, no. 6, June 1999, pages 1813-1818.	
	11.	Research Genetics, "Designer PCR," <i>Nucleic Acids Research</i> , vol. 22, no. 15, August 1994	
	12.	Sommer and Tautz, "Minimal homology requirements for PCR primers," <i>Nucleic Acids Research</i> , vol. 17, no. 16, page 6749, 1989	
	13.	Zaaijer et al., <i>Journal of Virological Methods</i> , vol. 52, 1995, pages 175-181	

Examiner Signature	/Bradley Sisson/	Date Considered	11/26/2007
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /BLS/

Receipt date: 07/25/2005

11108233 - GAU: 1634



INFORMATION DISCLOSURE CITATION PTO-1449	Attorney Docket No. 9310-22CT T/97300-US	Serial No. 11/108,233 09/463,352
	Applicant GOUDSMIT ET AL.	
	Filing Date JANUARY 21, 2000 April 18, 2005	Group 1655

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	AA					
	AB					
	AC					
	AD					
	AE					

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Translation

OTHER DOCUMENTS

	AJ	TEGLEJAERG ET AL., "Sensitive non-radioactive detection of HIV-1: use of nested primers for the amplification of HIV DNA" Molecular and Cellular Probes (1992) 6: p. 175-180
	AK	"Quantification of HIV-1 Using Multiple Competitors in a Single-Tube Assay" BioTechniques, vol. 21, no. 2 (1996) p. 248-255
	AL	ZAZZI ET AL., "Nested Polymerase Chain Reaction for Detection of Human Immunodeficiency Virus Type 1 DNA in Clinical Specimens" Journal of Medical Virology 32: (1992) p. 172-174
	AM	ENGELBRECHT ET AL., "Detection of Southern African human immunodeficiency virus type 1 subtypes by polymerase chain reaction: evaluation of different primer pairs and conditions" Journal of Virological Methods, 55 (1995) p. 391-400
	AN	INNOCENTI ET AL., "HIV-1 in Blood Monocytes: Frequency of Detection of Proviral DNA using PCR and Comparison with the Total CD4 Count" AIDS Research and Human Retroviruses, vol. 8, no. 2, (1992) p. 261-268
	AO	OTTMANN ET AL., "The Polymerase chain reaction for the detection of HIV-1 genome RNA in plasma from infected individuals" Journal of Virological Methods, 31 (1991) p. 273-284
	AP	QUIROS ET AL., "Human immunodeficiency virus type-1 can be detected in monocytes by polymérase chain reaction" J. Med. Microbiol., vol. 42, (1995) p. 411-414
	AQ	MCCUTCHAN ET AL., "Genetic Comparison of Human immunodeficiency Virus (HIV-1) Isolates by Polymerase Chain Reaction" Journal of Acquired Immune Deficiency Syndrome 4, (1991) p. 1241-1250
	AR	

Examiner

/Bradley Sisson/

Date Considered

11/26/2007

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Receipt date: 07/25/2005

11108233 - GAU: 1634

Sheet 1 of 2



FORM PTO-1449 U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket Number ~~9310-22EX~~
9310-22CT

Serial No.
09463352
11/108,233



LIST OF DOCUMENTS CITED BY APPLICANT

(Use several sheets if necessary)

Applicants: Goudsmit et al.

Filing Date: January 21, 2000
April 18, 2005

Group
1634

U. S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
BTA	1.	5,576,176	11/19/1996	Adams et al.			
BTA	17.	5,629,413	05/13/1997	Peterson et al.			

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes No
BTA	2.	EP 0 887 427 A2	12/30/1998	EPO			
	3.	EP 0 727 497 A1	08/21/1996	EPO			
	4.	EP 0 617 132 A3	09/28/1994	EPO			
	18. ✓	EP 0 402 997 A3	12/19/1990	EPO			
	19. ✓	EP 0 331 939 A3	09/13/1989	EPO			
BTA	20. ✓	WO 91/10746	07/25/1991	PCT			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

BTA	5.	Bell and Ratner "Specificity of Polymerase Chain Amplification Reactions for Human Immunodeficiency Virus Type 1 DNA Sequences" <i>AIDS Research and Human Retroviruses</i> 5(1):87-95 (1989)					
	6.	Böni et al. "PCR Identification of HIV-1 DNA Sequences in Brain Tissue of Patients with AIDS Encephalopathy" <i>Neurology</i> 43:1813-1817 (1993)					
	7.	Goto et al. "Detection of Proviral Sequences in Saliva of Patients Infected with Human Immunodeficiency Virus Type 1" <i>AIDS Research and Human Retroviruses</i> 7(3):343-347 (1991)					
	8.	Karikó "Identification of Conserved Sequences for PCR Primer Design by Multiple Alignments of Dot Matrix Plots" <i>BioTechniques</i> 18(6):1048-1049 (1995)					
	9.	Map of 5' LTR from HIV-1 reference genome (GenBank Accession No. K03455)					
	10.	Oehlschlager et al. "Detection of HIV-1 RNA by Nucleic Acid Sequence-Based Amplification Combined with Fluorescence Correlation Spectroscopy" <i>Proc. Natl. Acad. Sci. USA</i> 93:12811-12816 (1996)					
	11.	Scientific Report on Computer Analysis of the Alignment of the HIV LTR Sequence from the December 1996 Edition of the Human Retroviruses and AIDS Compendium published by the Los Alamos National Laboratory, New Mexico					
BTA	12.	Revels et al. "Comparative Evaluation of NASBA HIV-1 RNA QT, AMPLICOR-HIV Monitor, and QUANTIPLEX HIV RNA Assay, Three Methods for Quantification of Human Immunodeficiency Virus Type 1 RNA in Plasma" <i>Journal of Clinical Microbiology</i> 34(5):1058-1064 (1996)					

EXAMINER
EXAMINER

B. S. Sisson

DATE CONSIDERED

11/21/04

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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11/26/2007

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Receipt date: 07/25/2005

11108233 - GAU: 1634

Sheet 2 of 2

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office		Attorney Docket Number 9310-22CX 9310-22CT	Serial No. 09/463,352 11/108,233
LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary)		Applicants: Goudsmit et al.	
		Filing Date: January 21, 2000 April 18, 2005	Group 1634
B.L.L.	13.	LTR alignment from the December 1996 Edition of the Human Retroviruses and AIDS Compendium published by the Los Alamos National Laboratory, New Mexico	
	14.	Partial gag alignment from the December 1996 Edition of the Human Retroviruses and AIDS Compendium published by the Los Alamos National Laboratory, New Mexico	
	15.	Van Gemen et al. "Quantification of HIV-1 RNA in Plasma Using NASBA™ During HIV-1 Primary Infection" <i>Journal of Virological Methods</i> 43:177-188 (1993)	
B.L.L.	16.	File history of European patent application serial number EP 98943872.6, filed August 5, 1998	

/Bradley Sisson/

11/26/2007

EXAMINER
EXAMINER

B. L. Sisson

DATE CONSIDERED

11/21/04

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Receipt date: 07/25/2005



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INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	09/483,352 11/108,233
Filing Date	1/24/00 APR 18, 2005
First Named Inventor	Goudsmit
Group Art Unit	1855
Examiner Name	B. Sisson
Attorney Docket Number	9310-2 9310-22 CT

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
h528	1	6,001,558		Backus et al.	12/14/99	

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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Office	Number	Kind Code (if known)				

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T

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TC 1700

/Bradley Sisson/

11/26/2007

Examiner Signature	<i>Bradley Sisson</i>	Date Considered	11-15-02
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Receipt Date: 07/25/2005



11108233 - GAU: 1634
 09/463352
 420 Rec'd PCT/PTO 21 JAN 2000

INFORMATION DISCLOSURE CITATION	Atty Docket No. T/97300US 9310-22CT	Serial No. to be assigned 11/108,233
	Applicant GOUDSMIT ET AL	
PTO-1449	Filing Date April 18, 2005 21 JANUARY 2000	Group to be assigned 1655

U.S. PATENT DOCUMENTS

Examiner initial	Document Number	Date	Name	Class	Subclass	Filing Date	if Appropriate
<u>B1A</u>	AA US 5 629 413 A	09/13/89					
	AB						

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Translation
<u>31A</u> AJ EP 0 617 132A	09/28/94	EP	<u>Yes/No/Partial</u>
<u>84A</u> AK EP 0 331 939 A	09/13/89	EP	
<u>82A</u> AL EP 0 402 997 A	12/19/90	EP	
<u>82A</u> AN WO 91 10746 A	07/25/91	PCT	

OTHER DOCUMENTS

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 ____ | AP |
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 ____ | AS |

Examiner B. J. Sisson | Date Considered 2/12/00

/Bradley Sisson/

11/26/2007



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NOTICE OF ALLOWANCE AND FEE(S) DUE

20792 7590 12/12/2013
MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER

SISSON, BRADLEY L.

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 12/12/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814

TITLE OF INVENTION: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1780	\$0	\$0	\$1780	03/12/2014

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax **(571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

20792 7590 12/12/2013
MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814

TITLE OF INVENTION: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1780	\$0	\$0	\$1780	03/12/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
SISSON, BRADLEY L	1634	536-024330

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1	_____
2	_____
3	_____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

- ☐ Applicant certifying micro entity status. See 37 CFR 1.29
- ☐ Applicant asserting small entity status. See 37 CFR 1.27
- ☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see form PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmi	9310-22CT	5814

20792 7590 12/12/2013
MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER

SISSON, BRADLEY L.

ART UNIT PAPER NUMBER

1634

DATE MAILED: 12/12/2013

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 56 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 56 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notices of Allowance and Fee(s) Due mailed between October 1, 2013 and December 31, 2013

(Addendum to PTOL-85)

If the "Notice of Allowance and Fee(s) Due" has a mailing date on or after October 1, 2013 and before January 1, 2014, the following information is applicable to this application.

If the issue fee is being timely paid on or after January 1, 2014, the amount due is the issue fee and publication fee in effect January 1, 2014. On January 1, 2014, the issue fees set forth in 37 CFR 1.18 decrease significantly and the publication fee set forth in 37 CFR 1.18(d)(1) decreases to \$0.

If an issue fee or publication fee has been previously paid in this application, applicant is not entitled to a refund of the difference between the amount paid and the amount in effect on January 1, 2014.

Notice of Allowability	Application No. 11/108,233	Applicant(s) GOUDSMIT ET AL.	
	Examiner Bradley L. Sisson	Art Unit 1634	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendment filed 25 November 2013.
☐ A declaration(s)/affidavit(s) under 37 CFR 1.130(b) was/were filed on _____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are 36.41.46 and 58-60. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

- a) ☒ All b) ☐ Some *c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/463,352.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. ☐ Notice of References Cited (PTO-892) | 5. ☐ Examiner's Amendment/Comment |
| 2. ☐ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 6. ☐ Examiner's Statement of Reasons for Allowance |
| 3. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 7. ☐ Other _____ |
| 4. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____ | |

/Bradley L. Sisson/
Primary Examiner
Art Unit: 1634

Issue Classification 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.	
	Examiner BRADLEY L SISSON	Art Unit 1634	

US ORIGINAL CLASSIFICATION						INTERNATIONAL CLASSIFICATION									
CLASS		SUBCLASS				CLAIMED					NON-CLAIMED				
536		24.33				C	0	7	H	21 / 04 (2006.01.01)					
CROSS REFERENCE(S)						C	1	2	Q	1 / 70 (2006.01.01)					
						C	1	2	Q	1 / 68 (2006.01.01)					
						C	1	2	P	19 / 34 (2006.01.01)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					C	1	2	P	19 / 34 (2006.01.01)					
536	24.1	24.32													
435	5	6.12	91.2												
									</						

NONE		Total Claims Allowed:	
		6	
(Assistant Examiner) /BRADLEY L SISSON/ Primary Examiner, Art Unit 1634	(Date) 12/02/2013	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	-

Search Notes 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
435	5, 6, 91.1, 91.2, 91.21, 91.53, 183	6/22/2008	B.L.S.
536	23.1, 24.3, 24.33, 25.3,	6/22/2008	B.L.S.
436	94	6/22/2008	B.L.S.

SEARCH NOTES		
Search Notes	Date	Examiner
Sequence Search (Databases: GenEmbl, N_Geneseq, EST, Published, Issued, Pending)	1/25/2008	B.L.S.
EAST (see transcript for search terms and databases)	2/17/09	B.L.S.
STN, Registry file (SEQ ID NO: 1 & 5)	2/17/09	B.L.S.
Reviewed 11/372577	02/23/09	B.L.S.
EAST (see transcript for databases and search terms)	06/14/2013	B.L.S.
EAST 9see transcript for databases and search terms)	12/02/2013	B.L.S.

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
435	5, 6, 91.1, 91.2, 91.21, 183	6/22/2008	B.L.S.
536	24.33	6/22/2008	B.L.S.
Sequence Search		1/25/2008	B.L.S.

	/Bradley L Sisson/ Primary Examiner.Art Unit 1634
--	--

INTERFERENCE SEARCH

US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
EAST	See transcript for databases and search terms	12/02/2013	B.L.S.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	79	("HIV-1" "HTLV-III") and primer same (T3 T7 SP6) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 08:59
L3	1	("HIV-1" "HTLV-III") and primer same LTR same (T3 T7 SP6) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:00
L4	0	("HIV-1" "HTLV-III") and primer same (T3 T7 SP6) and "CTCAATAAAGCTTGCTTGA" and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:01
L5	0	("HIV-1" "HTLV-III") and primer and "CTCAATAAAGCTTGCTTGA" and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:01
L6	0	("HIV-1" "HTLV-III") and primer and ("GGGCGGCACTGCTAGAGA" "CTCAATAAAGCTTGCTTGA") and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:02
L7	0	("HIV-1" "HTLV-III") and ("GGGCGGCACTGCTAGAGA" "CTCAATAAAGCTTGCTTGA") and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:03
L8	0	("GGGCGGCACTGCTAGAGA" "CTCAATAAAGCTTGCTTGA") and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:03
L9	13	("HIV-1" "HTLV-III") same primer same (T3 T7 SP6) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:03
L10	7	("HIV-1" "HTLV-III") same primer with (T3 T7 SP6) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:03
L11	3	(\$GGGCGGCACTGCTAGAGA\$ \$CTCAATAAAGCTTGCTTGA\$) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:07

L12	1	(\$GGGCGGCACTGCTAGAGA\$ \$CTCAATAAAGCTTGCCTTGA\$) same primer and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/12/02 09:07
S1	6	"6881537"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/27 18:14
S2	11	"7056661"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/27 18:15
S3	49	"6232075"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/27 18:15
S4	1283	"5474796"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:55
S5	12	"5474796" and sisson	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:56
S6	22	"5403707"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:56
S7	43	"5472840"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2008/11/05 08:56
S8	6	"6881537"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/02/23 20:33
S9	0	WO9907898	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/10/28 15:19
S10	7	"9907898"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/10/28 15:19
S11	1	"9907898"	EPO	OR	OFF	2009/10/28 15:21
S12	19	"20010007747"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2009/10/29 17:35
S13	22	"5221610"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2011/01/17 14:03
S14	92	(variation variability) same ("HTLV- III" HIV AIDS) same (env LTR) and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/07/03 21:58
S15	1	(variation variability) same ("HTLV- III" HIV AIDS) same (env LTR) same primers and @pd<"19970808"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2012/07/03 21:59
S16	3	koroulis.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2012/07/12 17:10
S17	6070	promoter same (long length) with	US-PGPUB;	OR	OFF	2013/01/30

		(nucleotide base)	USPAT; EPO; JPO; DERWENT			08:20
S18	2551	promoter with (long length) with (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:21
S19	822	promoter with (long length) NEAR2 (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:21
S20	327	promoter NEAR4 (long length) NEAR2 (nucleotide base)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/01/30 08:22
S21	26	"5122457"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/01/30 08:30
S22	2	"20070048761"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/01/30 17:44
S23	491	(HIV "HIV-1" "HTLV-III" "AIDS virus") same provirus same sequence	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:25
S24	348	(HIV "HIV-1" "HTLV-III" "AIDS virus") same (provirus proviral) same sequence with DNA	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:26
S25	232	(HIV "HIV-1" "HTLV-III" "AIDS virus") with (provirus proviral) same sequence with DNA	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:26
S26	24	(HIV "HIV-1" "HTLV-III" "AIDS virus") with (provirus proviral) same sequence with DNA and @pd<"19970808"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 09:27
S27	3	koroulis.inv. and array	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 15:13
S28	52	\$CTCAATAAAGCTTGCTTGAS\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 17:26
S29	39	\$GGGCGGCGACTGCTAGAGAS\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 18:40
S30	16	\$GGGCGGCGACTGCTAGAGAS\$ and promoter with primer	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2013/06/14 18:52
S31	260	"6242568"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/17 09:53
S32	382	"6453242"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2013/06/17 10:25

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L13	1	(\$GGGGGGGCGGCTGCTAGAGAS\$ \$CTCAATAAAGCTTGCTTGA\$) same primer and @pd<"19970808"	USPAT; UPAD	OR	ON	2013/12/02 10:02
L14	13	("HIV-1" "HTLV-III") same primer same (T3 T7 SP6) and @pd<"19970808"	USPAT; UPAD	OR	ON	2013/12/02 10:04

12/ 2/ 2013 10:06:49 AM

C:\Users\bsisson\Documents\EAST\Workspaces\11108233.wsp

<i>Index of Claims</i> 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☒ T.D.		☐ R.1.47				
CLAIM		DATE								
Final	Original	10/04/2007	02/06/2008	06/22/2008	09/08/2008	02/23/2009	06/01/2009	09/09/2009	02/21/2010	12/02/2013
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<i>Index of Claims</i> 	Application/Control No. 11108233	Applicant(s)/Patent Under Reexamination GOUDSMIT ET AL.
	Examiner Bradley L Sisson	Art Unit 1634

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant		☐ CPA		☒ T.D.		☐ R.1.47				
CLAIM		DATE								
Final	Original	10/04/2007	02/06/2008	06/22/2008	09/08/2008	02/23/2009	06/01/2009	09/09/2009	02/21/2010	12/02/2013
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	39	÷	✓	-	-	-	-	-	-	-
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	43	÷	✓	-	-	-	-	-	-	-
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	47	÷	✓	-	-	-	-	-	-	-
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	55	÷	N	N	N	N	N	N	N	-
	56	÷	N	N	N	N	N	N	N	-
	57					✓	✓	-	-	-
2	58									=
4	59									=
6	60									=



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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BIB DATA SHEET

CONFIRMATION NO. 5814

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
11/108,233	04/18/2005	435	1634	9310-22CT
RULE				
APPLICANTS INVENTORS Jaap Goudsmit, Amsterdam, NETHERLANDS; Pieter Oudshoorn, Michielsgestel, NETHERLANDS; Suzanne Jurriaans, Monnickendam, NETHERLANDS; Vladimir Vladimirovich Lukashov, Dienen, NETHERLANDS;				
** CONTINUING DATA ***** This application is a CON of 09/463,352 01/21/2000 PAT 6881537 which is a 371 of PCT/EP98/04945 08/05/1998				
** FOREIGN APPLICATIONS ***** EUROPEAN PATENT OFFICE (EPO) 97202455.8 08/08/1997				
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/18/2005				
Foreign Priority claimed ☒ Yes ☐ No 35 USC 119(a-d) conditions met ☒ Yes ☐ No Verified and Acknowledged <u>/BRADLEY L SISSON/</u> Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY NETHERLANDS	SHEETS DRAWINGS 1	TOTAL CLAIMS 25 6
INDEPENDENT CLAIMS 6 3				
ADDRESS MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627 UNITED STATES				
TITLE NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1				
FILING FEE RECEIVED 2800	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:		☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit	

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: **Mail** **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

20792 7590 12/12/2013
MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/18/2005	Jaap Goudsmit	9310-22CT	5814

TITLE OF INVENTION: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1780	\$0	\$0	\$1780	03/12/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
SISSON, BRADLEY L	1634	536-024330

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

MYERS BIGEL SIBLEY & SAJOVEC, P.A.

- 1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

bioMerieux, B.V.

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Boxtel, Netherlands

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☒ Issue Fee
☒ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number 50-0220 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

- ☐ Applicant certifying micro entity status. See 37 CFR 1.29
- ☐ Applicant asserting small entity status. See 37 CFR 1.27
- ☐ Applicant changing to regular undiscounted fee status.

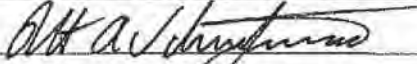
NOTE: Absent a valid certification of Micro-Entity Status (see form PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature



Date March 12, 2014

Typed or printed name Robert A. Schwartzman, Ph.D.

Registration No. 50,211

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Electronic Patent Application Fee Transmittal

Application Number:	11108233			
Filing Date:	18-Apr-2005			
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1			
First Named Inventor/Applicant Name:	Jaap Goudsmit			
Filer:	Robert Andrew Schwartzman/Marthenn Salazar			
Attorney Docket Number:	9310-22CT			
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl Issue Fee	1501	1	960	960
Publ. Fee- Early, Voluntary, or Normal	1504	1	0	0

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				960

Electronic Acknowledgement Receipt

EFS ID:	18443368
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Robert Andrew Schwartzman/Marthenn Salazar
Filer Authorized By:	Robert Andrew Schwartzman
Attorney Docket Number:	9310-22CT
Receipt Date:	12-MAR-2014
Filing Date:	18-APR-2005
Time Stamp:	13:48:32
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$960
RAM confirmation Number	59
Deposit Account	500220
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	32476 0de98eadb2e2995ea35a0bbbe247d25c1d6 68513	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			125072		
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.					



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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/108,233	04/15/2014	8697352	9310-22CT	5814

20792 7590 03/26/2014
MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 153 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

Jaap Goudsmit, Amsterdam, NETHERLANDS;
Pieter Oudshoorn, Michielsgestel, NETHERLANDS;
Suzanne Jurriaans, Monnickendam, NETHERLANDS;
Vladimir Vladimirovich Lukashov, Dienen, NETHERLANDS;

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Attorney Docket No. 9310-22CT

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.

U.S. Patent No.: 8,697,352

Application No.: 11/108,233

Issued: April 15, 2014

Filed: April 18, 2005

Confirmation No: 5814

Title: *NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1*

September 12, 2014

Commissioner for Patents

Attn: Certificate of Correction Branch

P.O. Box 1450

Alexandria, VA 22313-1450

**REQUEST FOR ENTRY OF CERTIFICATE OF CORRECTION
UNDER 35 U.S.C. §254 AND 37 C.F.R. §1.322**

Sir:

The Applicants of record for the above-referenced patent hereby request, pursuant to 35 U.S.C. §254 and 37 C.F.R. §1.322, that a Certificate of Correction be issued. This request is made in order to correct the mistakes incurred through the fault of the U.S. Patent and Trademark Office. The mistakes appearing in the patent are set forth with corrections on the Certificate of Correction attached herewith.

No fee is believed due. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



Robert A. Schwartzman
Registration No.: 50,211

Customer No.: 20792

Myers Bigel Sibley & Sajovec, P.A.

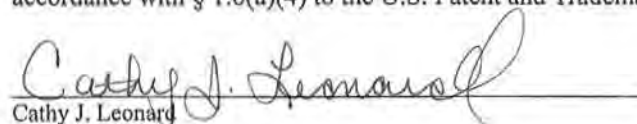
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Telephone: (919) 854-1400

Facsimile: (919) 854-1401

CERTIFICATION OF ELECTRONIC TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on September 12, 2014.


Cathy J. Leonard

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

Page 1 of 1

PATENT NO.: 8,697,352
APPLICATION NO.: 11/108,233
ISSUE DATE: April 15, 2014
INVENTOR(S): Goudsmit et al.

It is certified that an error appears or errors appear in the above-identified patent
and that said Letters Patent is hereby corrected as shown below:

In the Patent:

Column 11, Line 35: Please replace the entire line to read as follows:

Biotin probe: 5'- TGTTAAAAGAGACCATCAATGAGGA. SEQ ID 13

Column 11, Line 37: Please replace the entire line to read as follows:

ECL probe: 5' - GAATGGGATAGAGTGCATCCAGTG. SEQ ID 14

In the Claims:

Column 17, Claim 1, Lines 46 and 47:

Please correct "primer consists essentially of comprises a second"
to read -- primer consists essentially of a second --

Column 19, Claim 5, Lines 3 and 4:

Please correct "primer consists essentially of comprises a first"
to read -- primer consists essentially of a first --

Column 19, Claim 5, Line 10: Please correct "sequence of"

to read -- sequence of: --

MAILING ADDRESS OF SENDER:
Myers, Bigel, Sibley & Sajovec
P.O. Box 37428
Raleigh, NC 27627

Electronic Acknowledgement Receipt

EFS ID:	20119768
Application Number:	11108233
International Application Number:	
Confirmation Number:	5814
Title of Invention:	NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1
First Named Inventor/Applicant Name:	Jaap Goudsmit
Customer Number:	20792
Filer:	Robert Andrew Schwartzman/Cathy Leonard
Filer Authorized By:	Robert Andrew Schwartzman
Attorney Docket Number:	9310-22CT
Receipt Date:	12-SEP-2014
Filing Date:	18-APR-2005
Time Stamp:	10:26:52
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Certificate of Correction	9310-22CT_Request_for_COC.pdf	190052 #044b615f3de474b6e7191de4a3cd7258b67bca1	no	2

Warnings:

Information:

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 8,697,352 B2
APPLICATION NO. : 11/108233
DATED : April 15, 2014
INVENTOR(S) : Goudsmit et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Specification:

Column 11, Line 35: Please replace the entire line to read as follows:

Biotin probe: 5'- TGTTAAAAGAGACCATCAATGAGGA. SEQ ID 13

Column 11, Line 37: Please replace the entire line to read as follows:

ECL probe: 5' – GAATGGGATAGAGTGCATCCAGTG. SEQ ID 14

In the Claims:

Column 17, Claim 1, Lines 46 and 47:

Please correct “primer consists essentially of comprises a second”
to read -- primer consists essentially of a second --

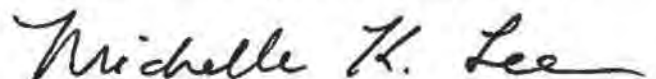
Column 19, Claim 5, Lines 3 and 4:

Please correct “primer consists essentially of comprises a first”
to read -- primer consists essentially of a first --

Column 19, Claim 5, Line 10:

Please correct “sequence of”
to read -- sequence of: --

Signed and Sealed this
Eighteenth Day of November, 2014



Michelle K. Lee
Deputy Director of the United States Patent and Trademark Office

TO: Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450	REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK
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In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been
 filed in the U.S. District Court Middle on the following ☒ Patents or ☐ Trademarks:

DOCKET NO. 1:17CV102	DATE FILED 2/3/2017	U.S. DISTRICT COURT Middle
PLAINTIFF BIOMERIEUX, INC., ET AL.		DEFENDANT HOLOGIC, INC., ET AL.
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 SEE ATTACHED		
2 8697352		
3 9074262		
4		
5		

In the above—entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1		
2		
3		
4		
5		

In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT		
CLERK John S. Brubaker	(BY) DEPUTY CLERK <i>Michelle L. Coyne</i>	DATE 2/3/2017

Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
 Copy 2—Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy