EXHIBIT 25

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

CONTROL NO.	FILING DATE	PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
95/000,527	01/13/10	7598035	

VINSON & ELKINS, LLP
FIRST CITY TOWER
1001 FANNIN STREET
SUITE 2500
HOUSTON, TX 77002-6760

EXAMINER	
TURNER,SHARON L.	
ART UNIT	**PAPER**
3991	

DATE MAILED:

03/24/10

INTER PARTES REEXAMINATION COMMUNICATION

BELOW/ATTACHED YOU WILL FIND A COMMUNICATION FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE OFFICIAL(S) IN CHARGE OF THE PRESENT REEXAMINATION PROCEEDING.

All correspondence relating to this *inter partes* reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this communication.



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.
95/000,527	01/13/2010	7598035	INV850/4-047REUS	8412

79975 7590 03/24/2010

King & Spalding LLP
P.O. Box 889
Belmont, CA 94002-0889

EXAMINER	
TURNER, SHARON L	
ART UNIT	PAPER NUMBER
3991	
MAIL DATE	DELIVERY MODE
03/24/2010	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.

RECEIVED
MAR 29 2010
IP DOCKET OFFICE
VINSON & ELKINS

Transmittal of Communication to Third Party Requester Inter Partes Reexamination	Control No.	Patent Under Reexamination	
	95/000,527	7598035	
	Examiner	Art Unit	
	SHARON L. TURNER	3991	

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

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

ORDER GRANTING/DENYING REQUEST FOR* INTER PARTES *REEXAMINATION	**Control No.**	**Patent Under Reexamination**	
	95/000,527	7598035	
	Examiner	**Art Unit**	
	SHARON L. TURNER	3991	

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

The request for *inter partes* reexamination has been considered. Identification of the claims, the references relied on, and the rationale supporting the determination are attached.

Attachment(s): ☐ PTO-892 ☒ PTO/SB/08 ☐ Other: _____

1. ☒ The request for *inter partes* reexamination is GRANTED.

   ☒ An Office action is attached with this order.

   ☐ An Office action will follow in due course.

2. ☐ The request for *inter partes* reexamination is DENIED.

This decision is not appealable. 35 U.S.C. 312(c). Requester may seek review of a denial by petition to the Director of the USPTO within ONE MONTH from the mailing date hereof. 37 CFR 1.927. EXTENSIONS OF TIME ONLY UNDER 37 CFR 1.183. In due course, a refund under 37 CFR 1.26(c) will be made to requester.

All correspondence relating to this *inter partes* reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this Order.

Inter Partes Reexamination

Order Granting Inter Partes Reexamination

1. A Request for *inter partes* reexamination of claims 1-5 of U.S. Patent No. 7,598,035 ('035) patent was filed 1-13-10 by a third party requestor.

2. A substantial new question of patentability (SNQ) affecting claims 1-5 of U.S. Patent No. 7,598,035 ('035) is raised by the request for reexamination.

Substantial New Question of Patentability

3. The presence or absence of "a substantial new question of patentability" (SNQ) determines whether or not reexamination is ordered.

For a "substantial new question of patentability" to be present, it is only necessary that:

A) the prior art patents and/or printed publications raise a substantial new question of patentability for at least one claim, such that a reasonable examiner would consider the teaching to be important in deciding whether or not the claim was patentable. A SNQ may be based on newly cited art or even solely on old art where the old art is being presented/viewed in a new light, or in a different way, as compared with its use in earlier concluded examination(s), in view of a material new argument or interpretation presented in the request. (MPEP 2242).

B) the same question of patentability as to the claim has not been decided by the Office in a previous examination or pending reexamination of the patent or in a final holding of invalidity by the Federal Courts, after appeals, or time for such have expired.

Documents Cited in the Request

Mandecki and Boiling, "FokI method of gene synthesis" Gene 68:101-107 (1988) (Mandecki).

Szybalski *et al.*, "Class-IIS restriction enzymes - a review" Gene 100:13-26 (1991) (Szybalski).

U.S. Patent No. 5,827,704 (Cease I).

Cease and Lohff, "A vector for facile PCR product cloning and modification generating any desired 4-base 5' overhang: pRPM" BioTechniques 14:250-255 (1993) (Cease II).

Dobrynin *et al.*, "Plasmid vectors pBBV for cloning and regeneration of DNA fragments with any end nucleotide sequence" Reports of the USSR Academy of Sciences 278:1002-1005 (1984) (Dobrynin).

Kuznedelov *et al*, "Plasmid vector pSSCI for cloning synthetic polynucleotides and their regeneration with a unique terminal nucleotide sequence" Bioorganic Chemistry 12:842-844 (1986) (Kuznedelov).

Palzkill and Botstein, "Probing 13-1actamase structure and function using random replacement mutagenesis" Proteins 14:29-44 (1992) (Palzkill).

U.S. Patent No. 5,677,153 (Botstein).

Mormeneo *et al*, "Precise nucleotide sequence modifications with bidirectionally cleaving class-IIS excision linkers" Gene 61:21-30 (1987) (Mormeneo).

Poustka *et al*, "Construction and use of human chromosome jumping libraries from NotI-digested DNA" Nature 325:353-355 (1987) (Poustka I).

Poustka and Lehrach, "Jumping libraries and linking libraries: the next generation of molecular tools in mammalian genetics" Trends in Genetics 2:174-179 (1986) (Poustka II).

Sapolsky and Lipshutz, "Mapping genomic library clones using oligonucleotide arrays" Genomics 33:445-456 (1996) (Sapolsky I).

U.S. Patent No. 5,710,000 (Sapolsky II).

Velculescu *et al.*, "Serial analysis of gene expression" Science 270:484-487 (1995) (Velculescu).

Discussion of the Documents Cited in the Request

4. Mandecki

The request proposes that a substantial new question of patentability as to claims 3-4 is raised by Mandecki (SNQ 1) and that a substantial new question of patentability as to claims 1-5 is raised by the reference in various combinations, see analysis below with respect to SNQ's 10, 19-21, 30-32, 41, and 50.

Mandecki is newly cited. Mandecki teaches a method for gene synthesis utilizing puc vectors with Fok I restriction sites on both sides of the inserted sequence, see Abstract, Figure 1 and Figures 3-4. Fok I makes a staggered double strand break at a DNA site 9 and 13 nt away from its recognition site. Upon cleavage of the plasmid DNA with FokI, a restriction fragment is liberated that by design contains unique 4-nt-long 5'-protruding ends. The uniqueness of ends permits efficient and directed simultaneous ligation of several restriction fragments to form a gene, see Abstract. Cloning may utilize any one of the pWM500 series of plasmids containing a unique Sma I insert cloning site flanked by two Fok I sites as well as other restriction cloning sites, See Figure 3. A cloning example of a gene fragment encoding the N-terminal portion of the p41 protein fo the HIV virus assembled by ligations of six separate DNA segments is provided, see Figure 4.

There is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether claims 1-5 of the '035 patent are patentable. The teachings of the Mandecki reference were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Mandecki reference alone and in combination raises a substantial new question of patentability as to claims 1-5 which has not been decided in a previous examination of the '035 patent.

5. Szybalski.

The request proposes that a substantial new question of patentability as to claims 3-4 is raised by Szybalski (SNQ 2) and that a substantial new question of patentability as to claims 1-5

is raised by the reference in combination, see analysis below with respect to SNQ's 11, 22, 33, 42, and 51.

Szybalski is newly cited. Szybalski teaches type IIs restriction endonuclesases and various cloning applications including their use in cloning procedures. The techniques include the preparation of DNA inserts and various vector constructs as well as plasmid linearization and ligation, see Abstract, Table I and Figures 1-7. Figure 5 particularly teaches vector constructs which accept fragments with two Fok I restriction sites adjacent to each side of the cloned DNA insert.

There is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not claims 1-5 of the '035 patent are patentable. The teachings of Szybzlski were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Szybalski reference alone and in combination raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

6. Cease I.

The request proposes that a substantial new question of patentability as to claims 3-4 is raised by Cease I (SNQ3) and that a substantial new question of patentability as to claims 1-5 is raised by the reference in combination, see analysis below with respect to SNQ's 12, 23, 34, 43, and 52.

Cease I is newly cited. Cease I teaches vectors with multiple copies of type IIs restriction endonucleases for cloning and modifying DNA fragments, see Abstract and Figures 1-2. The

orientation places the DNA insert internal to flanking Fok I and Bbs I sites. The vectors are noted to generate any 4 base 5' overhang desired.

There is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not claims 1-5 of the '035 patent are patentable. The teachings of the Cease I reference were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Cease I reference alone and in combination raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

7. Cease II.

The request proposes that a substantial new question of patentability as to claims 3-4 is raised by Cease II (SNQ 4)and that a substantial new question of patentability as to claims 1-5 is raised by the reference in combination, see analysis below with respect to SNQ's 13, 24, 35, 44, and 53.

Cease II is newly cited. The teachings of Cease II are similar to that of Cease I above. In particular the reference teaches RPM vectors for easy PCR product cloning and modification which generates any 4 base nucleotide sequence desirable in the 5' overhang. As depicted in Figures 1-2 the cloned DNA is inserted between two sets of type IIs restriction endonuclease sites, Fok I and BbsI.

There is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not claims 1-5 of the '035 patent are patentable. These teachings were not considered during the prosecution of the application which became the

'035 patent. Accordingly, the newly raised Cease II reference alone and in combination raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

8. Dobrynin.

The request proposes that a substantial new question of patentability as to claims 3-4 is raised by Dobrynin (SNQ 5) and that a substantial new question of patentability as to claims 1-5 is raised by the reference in combination, see analysis below with respect to SNQ's 14, 25, 36, 45, and 54.

Dobrynin is newly cited. Dobrynin teaches pBBV vectors with type IIs restriction sites BbvII flanking the 5' and 3' ends of insert DNA, see Figures 1-2. The vectors allow cloning and regeneration of DNA fragments with any end sequence.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Dobrynin reference were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Dobrynin reference alone and in combination raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

9. Kuznedelov.

The request proposes that a substantial new question of patentability as to claims 3-4 is raised by Kuznedelov (SNQ 6) and that a substantial new question of patentability as to claims 1-

5 is raised by the reference in combination, see analysis below with respect to SNQ's 15, 26, 37, 46, and 55.

Kuznedelov is newly cited. Kuznedelov teaches plasmid vector pSSCI with polylinker for cloning and regeneration of unique terminal nucleic acid sequences, see Figures 1-2. The DNA insert is flanked by two pairs of type IIs restriction endonucleases FokI and HgaI.

There is a substantial likelihood that a reasonable examiner would consider the teachings of Kuznedelov important in deciding whether or not the '035 claims are patentable. The teachings of Kuznedelov were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Kuznedelov reference alone and in combination raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

10. Palzkill.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Pazlkill.

Palzkill is newly cited. Palzkill teaches DNA cloning vectors with an excision linker and flanking BspMI (type IIs) restriction sites, see Figures 1-2. Palzkill utilizes the vector system to map genetic variations permitted within the TEM-1 β-lactamase gene. The cloning procedures include linearization of vectors and ligation.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Palzkill reference were not considered during the prosecution of the application

which became the '035 patent. Accordingly, the newly raised Palzkill reference raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

11. Botstein.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Botstein.

Botstein is newly cited. Botstein teaches cloning methods to modify target DNA. The method uses excision and mutation linkers to create defined deletions, see column 3, lines 20-43, column 5, lines 57-60 and Figures 1-7. The excision linker is flanked by two type IIs restriction sites. The cloning procedures include modification of DNA via successive treatments of insertion and removal of excision and mutation linker and ligation to form any desired fragment, see Summary, column 3, line 9-column 5, line 28. The procedures may be repeated so as to results in concatenation of any number of desired segments.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider the Botstein teachings important in deciding whether or not the '035 claims are patentable. The teachings of Botstein were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Botstein reference raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

12. Mormeneo.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Mormeneo.

Mormeneo is newly cited. Mormeneo teaches precise nucleotide sequence modifications with bidirectionally cleaving class IIs excision linkers, see Abstract. The resulting plasmid vehicles contain flanking BspMI (type IIs) restriction sites. Cloning procedures are demonstrated for modification of ampicillin Ap and tetracycline Tc resistance genes within vector pBR322.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Mormeneo reference were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Mormeneo reference raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

13. Poustka I.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Poustka I in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo, see SNQ's 10-18.

Poustka I is newly cited. Poustka I teaches molecular cloning and sequencing via the technique of DNA jumping libraries. In jumping libraries, large segments of DNA are deleted with the exception of the extreme ends. The multiple clones form a map, see Abstract, Figures 1-4.

The teachings of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein and Mormeneo which raise an SNQ are addressed above.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Poustka I reference in combination with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Poustka I reference in combination with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

14. Poustka II.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Poustka II in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo, see SNQ's 21-29.

Poustka II is newly cited. Poustka II teaches molecular cloning and sequencing techniques of DNA jumping libraries and DNA linking libraries, see Abstract and Figures 2-6. The Poustka II method involves generating large DNA fragments which are ligated to a marker plasmid and circularized, see p. 174, column 2 to p. 175, column 1. The marker plasmid and ligated DNA fragment are digested with a restriction enzyme then ligated with a phage vector. The resulting clones exhibit flanking restriction sites for subsequent sequencing, cloning and mapping, see particularly Figure 5.

The teachings of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein and Mormeneo which raise an SNQ are addressed above.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Poustka II reference in combination with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Poustka II reference in combination with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

15. Sapolsky I.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Sapolsky I in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo, see SNQ's 32-40. The request also proposes that a substantial new question of patentability is raised by Poustka I or Poustka II in combination with Sapolsky I and Mandecki, see SNQ's 19 and 30.

Sapolsky I is newly cited. Sapolsky I teaches mapping genomic clones using oligonucleotide arrays, see Abstract. Ambiguous sequences lying adjacent to a given Type IIS restriction site are ligated between two DNA adapters. These markers, once amplified and labeled by PCR, can be hybridized and detected on a high-density oligonucleotide array bearing

probes complementary to all possible markers. As seen in Figure 1 and 9, the DNA segments are flanked by type IIs restriction sites.

The teachings of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein, Mormeneo, Pousktka I and Poustka II which raise an SNQ are addressed above.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Sapolsky I reference in the above combinations with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein, Mormeneo, Pousktka I and Poustka II were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Sapolsky I reference in the above combinations with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein, Mormeneo, Pousktka I and Poustka II raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

16. Sapolsky II.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Sapolsky II in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo, see SNQ's 41-49. The request also proposes that a substantial new question of patentability is raised by Poustka I or Poustka II in combination with Sapolsky II and Mandecki, see SNQ's 20 and 31.

Sapolsky II is newly cited. Sapolsky II teaches capturing genomic sequences adjacent to type IIs restriction sites for genomic library mapping, see Abstract, Figures 1-3 and 8. The clones are adjoined with flanking adapter sequences and the internal sequence is determined and mapped, See column 3, lines 64-column 4, line 28 and column 6, line 24-32. The cloning procedure positions plasmid vectors with large DNA segments flanked by type IIs restriction sites.

The teachings of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein, Mormeneo, Pousktka I and Poustka II which raise an SNQ are addressed above.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Sapolsky II reference in the above combinations with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein, Mormeneo, Pousktka I and Poustka II were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Sapolsky II reference in the above combinations with Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein, Mormeneo, Pousktka I and Poustka II raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

17. Velculescu.

The request proposes that a substantial new question of patentability as to claims 1-5 is raised by Velculescu in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo, see SNQ's 50-58.

Velculescu teaches a DNA cloning procedure termed serial analysis of gene expression to analyze gene expression in various organisms and/or tissues. In the procedure, cDNA is ligated via anchoring restriction sites to linkers containing type IIS restriction sites (tagging enzymes). The linkers are designed so that cleavage of the ligation products with the tagging enzyme results in release of the linker with a short piece of the cDNA. Ligated tags serve as a template for PCR amplification and cleavage of the PCR product with the anchoring enzyme allows isolation of ditags that are linked by ligation, cloned, and sequenced. The orientation places desired segments adjacent each other and with flanking type IIs sites.

The teachings of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein and Mormeneo which raise an SNQ are addressed above.

It is agreed that there is a substantial likelihood that a reasonable examiner would consider these teachings important in deciding whether or not the '035 claims are patentable. The teachings of the Velculescu reference in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo were not considered during the prosecution of the application which became the '035 patent. Accordingly, the newly raised Velculescu reference in combination with any one of Mandecki, Szybalski, Cease I, Cease II, Dobrynin, Kuznedelov, Palzkill, Botstein or Mormeneo raises a substantial new question of patentability as to claims 1-5, which has not been decided in a previous examination of the '035 patent.

Conclusion

Inter Partes Duty to Disclose

18. The patent owner is reminded of the continuing responsibility under 37 CFR 1.985(a) to apprise the Office of any litigation activity, or other prior or concurrent proceeding, involving Patent No. 7,598,035 throughout the course of this reexamination proceeding. The third party requester is also reminded of the ability to similarly apprise the Office of any such activity or proceeding throughout the course of this reexamination proceeding.

Inter Partes Service of Papers

19. After the filing of a request for reexamination by a third party requester, any document filed by either the patent owner or the third party requester must be served on the other party (or parties where two or more third party requester proceedings are merged) in the reexamination proceeding in the manner provided in 37 CFR 1.248. See 37 CFR 1.903.

Amendment in Reexamination Proceedings

20. Patent owner is notified that any proposed amendment to the specification and/or claims in this reexamination proceeding must comply with 37 CFR 1.530(d)-(j), must be formally presented pursuant to 37 CFR 1.52(a) and (b), and must contain any fees required by 37 CFR 1.20(c).

Future Correspondence

21. **All** correspondence relating to this *inter partes* reexamination proceeding should be directed as follows:

By EFS to: Registered users may submit via the electronic filing system EFS-Web at https://sportal.uspto.gov/authenticate/authenticateuserlocalepf.html

By U.S. Postal Service Mail to:

Mail Stop *Inter partes* Reexam
ATTN: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

By FAX to: (571) 273-9900
Central Reexamination Unit

By hand to: Customer Service Window
Randolph Building
401 Dulany St.
Alexandria, VA 22314

/Sharon L. Turner, Ph.D./
Primary Examiner, CRU 3991

Conferee: /Brenda Brumback/
Primary Examiner, CRU 3991

Conferee: /Bruce Campell/
Primary Examiner, CRU 3991

DEBORAH D. JONES
CRU SPE-AU 3991

EXHIBIT 26

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

CONTROL NO.	FILING DATE	PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
95/000,527	01/13/10	7598035	

VINSON & ELKINS, LLP
FIRST CITY TOWER
1001 FANNIN STREET
SUITE 2500
HOUSTON, TX 77002-6760

EXAMINER
TURNER,SHARON L.

ART UNIT	PAPER
3991	

DATE MAILED:

03/24/10

INTER PARTES REEXAMINATION COMMUNICATION

BELOW/ATTACHED YOU WILL FIND A COMMUNICATION FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE OFFICIAL(S) IN CHARGE OF THE PRESENT REEXAMINATION PROCEEDING.

All correspondence relating to this *inter partes* reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this communication.

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.
95/000,527	01/13/2010	7598035	INV850/4-047REUS	8412

79975 7590 03/24/2010

King & Spalding LLP
P.O. Box 889
Belmont, CA 94002-0889

EXAMINER	
TURNER, SHARON L	
ART UNIT	**PAPER NUMBER**
3991	

MAIL DATE	DELIVERY MODE
03/24/2010	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.

Transmittal of Communication to Third Party Requester Inter Partes Reexamination	Control No.	Patent Under Reexamination	
	95/000,527	7598035	
	Examiner	Art Unit	
	SHARON L. TURNER	3991	

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

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

OFFICE ACTION IN* INTER PARTES *REEXAMINATION	**Control No.** 95/000,527	**Patent Under Reexamination** 7598035	
	Examiner SHARON L. TURNER	**Art Unit** 3991	

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

Responsive to the communication(s) filed by:
Patent Owner on _____
Third Party(ies) on _____

RESPONSE TIMES ARE SET TO EXPIRE AS FOLLOWS:

For Patent Owner's Response:
2 MONTH(S) from the mailing date of this action. 37 CFR 1.945. EXTENSIONS OF TIME ARE GOVERNED BY 37 CFR 1.956.
For Third Party Requester's Comments on the Patent Owner Response:
30 DAYS from the date of service of any patent owner's response. 37 CFR 1.947. NO EXTENSIONS OF TIME ARE PERMITTED. 35 U.S.C. 314(b)(2).

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this Office action.

This action is not an Action Closing Prosecution under 37 CFR 1.949, nor is it a Right of Appeal Notice under 37 CFR 1.953.

PART I. THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892
2. ☒ Information Disclosure Citation, PTO/SB/08
3. ☐ _____

PART II. SUMMARY OF ACTION:

1a. ☒ Claims 1-5 are subject to reexamination.
1b. ☐ Claims _____ are not subject to reexamination.
2. ☐ Claims _____ have been canceled.
3. ☐ Claims _____ are confirmed. [Unamended patent claims]
4. ☐ Claims _____ are patentable. [Amended or new claims]
5. ☒ Claims 1-5 are rejected.
6. ☐ Claims _____ are objected to.
7. ☐ The drawings filed on _____ ☐ are acceptable ☐ are not acceptable.
8. ☐ The drawing correction request filed on _____ is: ☐ approved. ☐ disapproved.
9. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119 (a)-(d). The certified copy has: ☐ been received. ☐ not been received. ☐ been filed in Application/Control No _____.
10. ☐ Other _____

Inter Partes Reexamination

First Action on the Merits

1. A Request for *inter partes* reexamination of claims 1-5 of U.S. Patent No. 7,598,035 ('035) patent was filed 1-13-10 by a third party requestor.

2. An order granting *inter partes* reexamination of claims 1-5 of the '035 patent is transmitted herewith.

The '035 Patented Claims

3. The '035 patent consists of claims 1-5. Claims 1 and 3 are independent and are appended below.

1. A method of forming a linked pair of segments from each fragment of a population of polynucleotide fragments, wherein each said fragment is in a vector, said vector comprises two type IIs restriction endonuclease recognition sites, one of said type IIs restriction endonuclease recognition sites is adjacent to one end of the fragment and another of said type IIs restriction endonuclease recognition sites is adjacent to another end of the fragment, and one or more type IIs restriction endonucleases recognizing said type IIs restriction endonuclease recognition sites have two cleavage sites within the interior of the fragment, the method comprising:

treating each said vector and fragment with said one or more type IIs restriction endonucleases recognizing said type IIs restriction recognition sites, such that each fragment is cleaved at said cleavage sites, thereby removing the region of the fragment between said cleavage sites, whereby a pair of segments from said fragment remain connected to each other via said vector after said removing and each of said segments has a cleaved end; and

ligating together the cleaved ends produced by said removing thereby forming a linked pair of segments from each said fragment.

3. A method of forming linearized vectors having pairs of segments from a population of polynucleotide fragments, the method comprising the steps of:

i) inserting each of said polynucleotide fragments from said population into a vector having two type IIs restriction endonuclease recognition sites and forming vectors containing said polynucleotide fragments such that each of the vectors containing said polynucleotide fragments comprises a fragment from said population of polynucleotide fragments, one of said type IIs restriction endonuclease recognition sites in each of the vectors containing said polynucleotide fragments is adjacent to one end of the fragment and another of said type IIs endonuclease recognition sites in each of the vectors containing said polynucleotide fragments is adjacent to another end of the fragment, and one or more type IIs restriction endonucleases

recognizing said type IIs restriction endonuclease recognition sites have two cleavage sites within the interior of the fragment; and

ii) treating each of the vectors containing said polynucleotide fragments with said one or more type IIs restriction endonucleases recognizing the type IIs restriction endonuclease recognition sites and producing linearized vectors having pairs of segments wherein each of said linearized vectors having pairs of segments has a pair of segments of the fragment, one of said pair of segments is located at one end of each of the linearized vectors, and another of said pair of segments is located at another end of each of the linearized vectors.

Claim Interpretation

4. The '035 patent describes a mapping procedure comprised of captured end sequences of ordered restriction fragments. The procedure utilizes standard cloning procedures and vectors. While the patent claims are directed to various methods, the recited methods are not apparently directed to the full mapping procedure, but to various stages of cloning procedures which may be involved in such assembly.

A description of a preferred vector of the '035 patented invention is provided in Figure 2, see particularly type IIs restriction sites 204 and 212, and adjacent restriction sites 206 and 210 that permit cleavage of the vector and insertion of DNA fragment 208 by ligation, see also the '035 patent at column 6, line 22-50 for details. The orientation and location of restriction sites is such that the DNA inserts are provided without destroying the flanking IIs sites and such that cleavage with the IIs enzyme reaches over the insert site and occurs within the interior of the insert fragment. This is the general configuration of the vectors recited in the patented claims. It is noted that the internal cloning sites 206 and 210 are not required in the claims.

The above orientation is such that following ligation of DNA insert 208 into the vector, treatment with the flanking IIs endonucleases 204 and 212 effect cleavage consistent with the requirements of claim 1 i.e., "such that each fragment is cleaved at said cleavage sites; thereby removing the region of the fragment between said cleavage sites, whereby a pair of segments

from said fragment remain connected to each other via said vector after said removing and each of said segments has a cleaved end."

This configuration also provides an orientation such that following ligation of DNA insert (208) into the vector, treatment with the flanking IIs endonucleases 204 and 212 effect cleavage consistent with the requirements of claim 3 i.e., "having pairs of segments wherein each of said linearized vectors having pairs of segments has a pair of segments of the fragment, one of said pair of segments is located at one end of each of the linearized vectors and another of said pair of segments is located at another end of each of the linearized vectors."

As in Figure 2 and column 6, lines 51-61, the vector may also provide other restriction sites and/or associated primer sites. The specification further provides that any number of other type IIs sites may be present within the vector or insert, see Detailed Description of the Invention, column 4, line 10-column 9, line 26 and claims referencing "one or more" sites.

The method of claim 1 covers a method of forming linked pairs of segments by treating such vectors with one or more type IIs restriction endonucleases for cleavage and ligating the cleaved ends to form a linked pair of segments. Following such cleavage it is noted that linear vector is formed as well as removal of the cloned fragment. Both the vector and the fragment have cleaved ends and the subsequent ligation may occur at any of the respective ends. Accordingly, the claim encompasses situations where vector is religated with itself, with or without fragment, as well as where concatamers of vector and/or fragments may occur.

The method of claim 3 covers a method of forming linearized vectors. Step i) of the claim recites inserting a DNA fragment. This step corresponds to formation of a vector of the configuration discussed above, see Figure 2 and column 6, line 22-50 having a DNA insert 208

(fragment) inserted therein. Step ii) of claim 3 recites treating each vector with one or more type IIs endonucleases to produce linearization. While such cutting may remove the interior portion of the fragment insert, such is not required by the claim and the scope includes where the insert remains linked to the vector.

The claims refer to "pairs of segments from a population of polynucleotide fragments." The length of the fragments and segments are not particularly disclosed. Further, the pairs of segments need not be adjacent, particularly where, "one of said pair of segments is located at one end of each of the linearized vectors, an another of said pair of segments is located at another end of each of the linearized vectors," as in claim 3. While the specification discusses fragments with respect to "restriction fragments" and segments as portions of the restriction fragments, particularly end portions of restriction fragments, such qualifications are not recited within the claims. In addition, none of the "fragments" or "segments" requires any particular DNA sequence. Hence, it appears the "fragments" may be represented by 2-3 or more nucleotide bases and the "segments" may be represented by one or more nucleotide bases as long as they are in a configuration consistent with the other limitations of the claims.

Mapping and Cloning Strategies

5. Poustka I and II teach mapping techniques similar to that disclosed in the '035 patent by capturing end segments of various restriction fragments. However, the procedure is not disclosed as utilizing type IIs restriction sites.

6. Sapolsky I and II also teach mapping techniques similar to that disclosed in the '035 patent by capturing end segments of various restriction fragments. Sapolsky I and II utilize type IIs restriction sites as well as ligation with a type IIs adapter. The orientation places the fragment

between two type IIs sites consistent with the orientation of the vectors claimed and cleavage is into the desired fragment. In the Sapolsky I and II procedure, the segment may be reproduced by amplification rather than cloning and sequence analysis may proceed via hybridization to oligonucleotide arrays.

7. Velculescu also teaches a mapping procedure similar to that disclosed in the '035 patent which captures end sequences of restriction fragments. In the Velculescu method the end sequences are arranged between two type IIs restriction sites which are assembled by ligating IIs linkers, See Figure 1. Cleavage is also internal to the desired fragment or segment. The sequences are cut and are then linked together by ligation. The concatenated sequences are amplified, cleaved, isolated, concatenated and cloned. This orientation is also consistent with the claimed vectors.

Documents Cited in this Office Action

Mandecki and Boiling, "FokI method of gene synthesis" Gene 68:101-107 (1988) (Mandecki).

Szybalski *et al.*, "Class-IIS restriction enzymes - a review" Gene 100:13-26 (1991) (Szybalski).

U.S. Patent No. 5,827,704 (Cease I).

Cease and Lohff, "A vector for facile PCR product cloning and modification generating any desired 4-base 5' overhang: pRPM" BioTechniques 14:250-255 (1993) (Cease II).

Dobrynin *et al.*, "Plasmid vectors pBBV for cloning and regeneration of DNA fragments with any end nucleotide sequence" Reports of the USSR Academy of Sciences 278:1002-1005 (1984) (Dobrynin).

Kuznedelov *et al*, "Plasmid vector pSSCI for cloning synthetic polynucleotides and their regeneration with a unique terminal nucleotide sequence" Bioorganic Chemistry 12:842-844 (1986) (Kuznedelov).

Palzkill and Botstein, "Probing 13-1actamase structure and function using random replacement mutagenesis" Proteins 14:29-44 (1992) (Palzkill).

U.S. Patent No. 5,677,153 (Botstein).

Mormeneo *et al,* "Precise nucleotide sequence modifications with bidirectionally cleaving class-IIS excision linkers" Gene 61:21-30 (1987) (Mormeneo)

Poustka *et al,* "Construction and use of human chromosome jumping libraries from NotI-digested DNA" Nature 325:353-355 (1987) (Poustka I).

Poustka and Lehrach, "Jumping libraries and linking libraries: the next generation of molecular tools in mammalian genetics" Trends in Genetics 2:174-179 (1986) (Poustka II).

Sapolsky and Lipshutz, "Mapping genomic library clones using oligonucleotide arrays" Genomics 33:445-456 (1996) (Sapolsky I).

U S Patent No. 5,710,000 (Sapolsky II).

Velculescu *et al* , "Serial analysis of gene expression" Science 270·484-487 (1995) (Velculescu)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language

Claim Rejections - 35 USC § 103

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 negatived by the manner in which the invention was made

Third Party Proposed Rejections

Ground 1. Rejection of claims 3-4 was proposed by the third party requester in the request for reexamination at p. 45, line 1-p. 46, line 24 and claim chart-A, which statements are incorporated herein by reference for the grounds of rejection. The rejection is adopted substantially as proposed with the following modifications. The rejection is further applied to claims 1-2 and 5 for the following reasons.

Thus, claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Mandecki.

Mandecki teaches artificial gene synthesis by insertion of gene fragments into plasmid DNA; see Abstract, lines 1-14. The procedure involves restriction endonuclease cutting to linearize plasmid vector and inserting the DNA to be cloned by ligating the DNA into the plasmid vector. The DNA inserts are bracketed by vector sequences comprising two arms which contain Fok I restriction sites, see particularly Figure 3 and plasmids pWM500, 501, 502 and 507. The plasmid vector is designed to receive inserts by restriction endonuclease cutting at an internal Sma I cloning site and cloning between the two Fok I sites. As further depicted in figures 1 and 2, treatment with Fok I results in reach over cleavage such that the insert is cut within the interior. Accordingly, the Mandecki vectors containing insert are in the configuration recited in independent claims 1 and 3. DNA insert is subsequently cleaved by restriction with Fok I thereby producing gene fragments with unique 4-nt protruding ends, see Figure 1 and text p. 102, column 1, line 27-column 2, line 18. Notably the vector also retains a portion of the interior fragment. This cleavage is consistent with the limitations of the treating step in claim 1 as well as in claim 3i).

As an example, Mandecki teaches assembly of a gene fragment encoding the N-terminal portion of the p41 protein of the HIV virus formed by ligation of six different restriction fragments that are subsequently cleaved, see Abstract, p. 105, column 1, line 22-column 2, line 25, p. 105, column 2, line 46-p. 106, column 1, line 4 and Figure 4. Thus, this ligation is consistent with the recitation of the ligating step in claim 1. The reference further notes that the method is not limited to directed ligation of Fok I restriction fragments introduced by bridge mutagenesis. Protruding ends with 5' overhangs may also be generated by Fok I digestion of any DNA cloned into the Sma I site, see p. 106, column 2, line 15-p. 107, column 1, line 9. Accordingly Mandecki teaches a method of forming linked pairs of segments comprising treating with one or more type IIs endonucleases, here Fok I, and ligating the cleaved ends as recited in claim 1. The plasmid further provides the same type IIs sites in accordance with claim 2.

As discussed by requester, Mandecki's examples include vectors with inserts of paired segments of polynucleotide fragments which are linearized by treatment with two Fok I type IIs endonucleases and thus meet the limitations of claims 3 and 4. Also consistent with claim 5, the cloning procedure and/or artificial gene synthesis procedure subsequently links such segments and re-circularizes vector by ligation, see Abstract, p. 102, column 2, lines 11-18, p. 103, column 2, lines 10-18, p. 105, column 2, lines 17-25.

Accordingly, the Mandecki reference anticipates claims 1-5.

Ground 2. Rejection of claims 3-4 was proposed by the third party requester in the request for reexamination at p. 46, line 25-p. 48, line 14 and claim chart-B, which statements are incorporated herein by reference for the grounds of rejection. The rejection is adopted

substantially as proposed with the following modifications. The rejection is further applied to claims 1-2 and 5 for the following reasons.

Thus, claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Szybalski.

Szybalski teaches type IIs restriction endonucleases, their cleavage and recognition sites, see Table 1. Szybalski also teaches cloning applications using vectors with type IIs restriction endonuclease sites as well as inserting or excising DNA fragments using Fok I sites and/or cleavage. Cleavage with Fok I generates 4 nt 5' ss ends which can be filled-in with Pollk in the presence of the required dNTPs. Although only one cut site on one strand is present in such truncated molecules, they are again cleaved by Fok I, releasing 4-nt oligos (Ki5). More surprisingly, filling-in with only 2 or 3 nt still provides a substrate for FokI, with the release of a di- or trinucleotide, see p. 17, lines 1-7. The techniques include the preparation of DNA inserts and gene assembly using trimming, excision linkers, restriction fragments, adapter sequences and/or amplification, see III. Unique Applications, p. 18, column 1, line 1-p. 23, column 2, line 13. Various vector constructs include one or more type IIs cleavage sites, including IIs sites flanking the DNA insert and cloning by restriction endonuclease digestion (such as for plasmid linearization or end cleavage) followed by subsequent ligation, see Abstract, Table I and Figures 1-8.

Figure 5 particularly teaches, "Cloning and a precise excision of DNA fragments with unique cohesive ends. The vector contains a specially designed cassette, with two class-IIS restriction sites facing each other and a unique site (Sma I) in between. (I) The plasmid was cut at the Sma I site. (2) The blunt-ended DNA fragment (bold letters) is cloned into the Sma I site. (3) Digestion of the plasmid with Fok I produces DNA fragments with unique cohesive ends derived from the insert DNA. Various plasmids containing cassettes analogous to the one shown here (pWM500, Ma1) were constructed (pZPI8, Pa1; pBBV, Ko4; pSSC1, Ka2). When using pWM500, any DNA fragment cloned into the Sma I site can be excised precisely with unique cohesive ends by FokI digestion; these can be ligated in a single step when constructing a gene. See Brl; Do2; Ko3; Ko4; Ka2; Mal; Pal; Spl; Url; Ve3; Ve4."

Accordingly Figures 5 teaches a vector consistent with the recitations of claims 1 and 3, see (c) precise excision, p. 20, column 1, lines 1-10 following Figure 5. As discussed above, cleavage with Fok I cuts the vector such that segments of the DNA insert are retained (remain connected to each other) in the vector. Consistent with claim 1, the method includes forming linked pairs of segments (for example when constructing a gene) from such vectors comprising treating with one or more IIs endonucleases and ligating the cleaved ends. Also consistent with claim 2, the plasmid provides the same type IIs (Fok I) sites flanking the DNA insert.

As discussed by requester, Figures 5 exemplifies formation of vectors by inserting paired segments of polynucleotide fragments which are linearized by treatment with two Fok I sites flanking the inserts and thus Mandecki teaches claims 3-4. Consistent with claim 5, the cloning procedure includes re-circularization by ligation, see Figure 5.

Therefore, the Szybalski reference anticipates claims 1-5.

Ground 3. Rejection of claims 3-4 was proposed by the third party requester in the request for reexamination at p. 48, line 15-p. 50, line 9 and claim chart-C, which statements are incorporated herein by reference for the grounds of rejection. The rejection is adopted substantially as proposed with the following modifications. The rejection is further applied to claims 1-2 and 5 for the following reasons.

Thus, claims 1-5 are rejected under 35 USC 102(e) as being anticipated by Cease I with further evidence from Mandecki.

Cease I teaches pRPM vectors with multiple copies of any type IIs restriction endonuclease for cloning and modification of DNA fragments, see Abstract, column 3, line 31-

column 6, line 41, Figures 1-2 and claims 8-10. The orientation places the DNA insert internal to flanking Fok I and Bbs I sites, and the Fok I site is oriented such that cleavage is internal to the DNA segment and reaches over the internal Sma I or Pml I insertion site, see for example column 4, lines 24-column 5, line 7. The vectors enable any desired four-base 5' overhang or one-base 3' overhang sequence and cloning in the reading frame of choice with lac Z, see Summary, column 2, lines 29-column 3, line 16. The vector inserts may be amplified and subsequently excised, thereby producing modified fragments free of vector sequences, see column 5, lines 11-column 6, line 4. Thus, the vector corresponds to the configuration recited in claims 1 and 3.

Cloning techniques may be applied with the vector system to provide linked pairs of segments of a population of polynucleotide fragments as in cloning, see column 5, lines 9-58. For example, Cease I teaches Fok I gene construction strategy, see reference to Mandecki (discussed above in Ground 1) at column 5, line 42-44. Such techniques also include reversible cloning as well as excision and fill-in reactions to regenerate the original fragment (or fragment ends) regardless of sequence. The fragments may be (re)generated for use in engineering DNA constructs, see Summary column 2, lines 29-column 3, line 16 and Figures 1-2. Thus Cease I teaches cutting such vectors, particularly with Fok I and ligating the cleaved ends as recited in claims 1, and the vector comprises two of the same Fok I sites as in claim 2.

As discussed by Requester, Figures 1 and 2 further teach formation of such vectors with inserts of paired segments of polynucleotide fragments that are linearized by treatment with one or more IIs endonucleases (Fok I) as recited in claims 3 and 4. Further regarding claim 5, the

cloning procedure includes re-circularization by ligation as when constructing a gene or reversible cloning, see column 2, lines 7-25, column 5, lines 9-58 and column 6, lines 33-41.

Accordingly, the Cease I reference teachings anticipate claims 1-5.

Ground 4. Rejection of claims 3-4 was proposed by the third party requester in the request for reexamination at p. 50, line 10-p. 52, line 2 and claim chart-D, which statements are incorporated herein by reference for the grounds of rejection. The rejection is adopted substantially as proposed with the following modifications. The rejection is further applied to claims 1-2 and 5 for the following reasons.

Thus, claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Cease II with further evidence of Mandecki.

The teachings of Cease II are similar to that of Cease I above. In particular the reference teaches RPM vectors for easy PCR product cloning and modification. The procedure generates any 4 base nucleotide sequence desirable in the 5' overhang. As depicted in Figures 1-2 the cloned DNA is inserted between two sets of type IIs restriction endonuclease sites, Fok I and Bbs I. As noted in the Abstract, "The vectors allow DNA to be cloned into a unique restriction site by blunt-end ligation or by AT-cloning. The cloned DNA is subsequently excised using class IIS restriction enzymes flanking the insert yielding a fragment that is entirely free of vector sequences. These enzymes recognize sequences in the vector but "reach-over" the junction to cut within the insert thereby generating a 4- base 5' overhang sequence determined by the 5' sequence of the insert. Thus, in cases where the insert was generated by PCR the overhangs are determined by the primer. More generally, these vectors offer a capability for reversible cloning

of any blunt DNA fragment because excision and fill-in reactions precisely regenerate the original blunt fragment regardless of its sequence." Accordingly, the Cease II vector corresponds to the configuration of claims 1 and 3.

Cease II exemplifies cloning of the Abelson gene, see p. 251, column 1-p. 254, column 1. The RPM vectors offer a general strategy for the reversible cloning of any blunt DNA. After blunt cloning into pRPMI or pRPM2, one can excise the insert with Bbs I and subsequently fill in the overhang to completely regenerate the original blunt fragment regardless of its sequence. No knowledge of the insert sequence is required and no vector-derived sequence is added. This novel and potentially useful capability is unique to the RPM vectors, see p. 255, column 1.

The Cease II pRPM1/ABL1 construct corresponds to the configuration recited in claim 1. The vector was cleaved by treatment with Bbs I and ligated into plasmids pMal-c and pMal-p. Thus Cease II meets the limitations of claims 1 and 2, see Cloning and Modification of an Abelson Oncogene Segment, p. 251, column 1, line 47-p. 254, column 1, line 46. In like manner, Cease II includes the above for the preparation of DNA fragments for use in engineering DNA constructs, see p. 254, column 2, line 11-p. 255, column 1, line 45. This includes use in the Fok I gene construction strategy (7), which is a reference to Mandecki discussed above in Ground 1.

As discussed by requester, the Cease II vectors are consistent with claims 3-4, having inserted therein the Abelson gene (i). Vector was treated with Bbs I for cleavage to form linearized vectors (ii). Further as to claim 5, the above re-circularization by ligation allows Fok I gene construction and regeneration of vector fragments as in reversible cloning, see Introduction p. 250, column 2, line 1-column 3, line 4.

Thus, the Cease II reference anticipates claims 1-5.

Ground 5. Rejection of claims 3-4 was proposed by the third party requester in the request for reexamination at p. 52, line 3-p. 53, line 21 and claim chart-E, which statements are incorporated herein by reference for the grounds of rejection. The rejection is adopted substantially as proposed with the following modifications. The rejection is further applied to claims 1-2 and 5 for the following reasons.

Thus, claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Dobrynin with further evidence of Kuznedelov.

Dobrynin teaches pBBV vectors with type IIs restriction sites Bbv II flanking the 5' and 3' ends of insert DNA, see Figures 1-2. The vectors allow cloning and regeneration of DNA fragments with any end sequence and with various modifications such that cloning may be in frame with expression of LacZ, see p. 1002, line 1-p. 1005, line 34. Accordingly, the Dobrynin pBBV vectors correspond to the configuration recited in claims 1 and 3, see Figures 1 and 2.

As in the last portion of Figure 1 and claim 1, the vector having a DNA inserted therein is cut by treatment with Bbv II to remove the internal region of the fragment. As noted at p. 1005, lines 28-34, the vector is suitable for cloning DNA fragments to be obtained by multicomponent ligation of synthetic oligonucleotides. Thus, Dobrynin teaches the limitations of claim 1 and 2 where the vector provides two flanking Bbv I, IIs sites. The vector allows cloning of various DNA fragments with subsequent regeneration from a recombinant plasmid independent of the sequence being cloned. The figure also notes this circular nature where cleaved vector is subsequently relegated. Thus in addition to anticipation of claims 3-4 as discussed by requester,

claim 5 directed to re-circularization of linearized vector is anticipated by Dobrynin. A further evidentiary example of the use of such vectors is evidenced in Kuznedelov discussed below.

Thus, claims 1-5 are anticipated by Dobrynin.

Ground 6. Rejection of claims 3-4 was proposed by the third party requester in the request for reexamination at p. 53, line 22-p. 55, line 16 and claim chart-F, which statements are incorporated herein by reference for the grounds of rejection. The rejection is adopted substantially as proposed with the following modifications. The rejection is further applied to claims 1-2 and 5 for the following reasons.

Thus, claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Kuznedelov with further evidence of Dobrynin.

Kuznedelov teaches cloning of genes via molecular subcloning. In the method vectors are utilized to subclone and purify separate fragments of the DNA from a gene. The fragments are subsequently purified and assembled by ligation as a full sequence. Kuznedelov acknowledges use of pBBV vectors to assemble such subcloned DNA fragments as a full sequence using cleavage with type IIs endonucleases BbvII, see p. 842, line 1-p. 844, line 11. The structure of the pBBV vectors is further evidenced in Dobrynin above. An example is referenced for cloning the gene that codes the virion protein VP1 of the hoof-and-mouth-virus. Thus, Kuznedelov teaches the general method of claim 1-2 involving linking pairs of segments via cutting such vectors with BbvII IIs endonucleases and ligating the cleaved ends.

Kuznedelov also teaches claims 1-2 via construction of plasmid vector pSSCI with a polylinker allowing for the cloned fragment to be inserted to sticky end restrictions sites rather

than blunt ended cloning, see Figures 1-2 and p. 844, lines 12-22. DNA fragments cloned at EcoRI and Pst I sites may be subsequently cleaved with Fok I and/or HgaI to provide fragments with the 5' overhang ends of the sequence which may be cross-linked into longer DNA (genes) by ligation, see p. 844, lines 23-28. The method provides for cloning and regeneration of unique terminal nucleic acid sequences for cloning and gene assembly via molecular subcloning, see Figures 1-2.

As further discussed by requester with respect to claims 3-4, the pSSCI plasmids of Kuznedelov have DNA inserts flanked by two pairs of type IIs restriction endonucleases Fok I and Hga I. Further as to claim 5, the method includes cloning linked pairs of segments by cleavage and subsequent ligation (as in gene assembly). Such allows construction of a cloned gene from such sub-cloned sequences, the vectors are re-circularized by ligation (claim 5) and the cloned gene sequence is regenerated, see p. 842-844 text. Thus, the Kuznedelov reference anticipates claims 1-5 of the '035 patent.

Ground 7. Claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Palzkill.

This rejection was proposed by the third party requester in the request for reexamination at p. 55, line 17-p. 59, line 8 and claim chart-G, which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 8. Claims 1-5 are rejected under 35 USC 102(a) and (e) as being anticipated by Botstein.

This rejection was proposed by the third party requester in the request for reexamination at p. 59, line 9-p. 63, line 14 and claim chart-H, which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 9. Claims 1-5 are rejected under 35 USC 102(b) as being anticipated by Mormeneo.

This rejection was proposed by the third party requester in the request for reexamination at p. 63, line 15-p. 67, line 15 and claim chart-I, which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 10. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 67, line 17-p. 73, line 15 and claim chart-J.1., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 11. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Szybalski.

This rejection was proposed by the third party requester in the request for reexamination at p. 73, line 16-p. 79, line 2 and claim chart-J.2., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 12. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Cease I.

This rejection was proposed by the third party requester in the request for reexamination at p. 79, line 3-p. 84, line 22 and claim chart-J.3., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 13. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Cease II.

This rejection was proposed by the third party requester in the request for reexamination at p. 84, line 23-p. 90, line 13 and claim chart-J.4., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 14. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Dobrynin.

This rejection was proposed by the third party requester in the request for reexamination at p. 90, line 14-p. 95, line 21 and claim chart-J.5., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 15. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Kuznedelov.

This rejection was proposed by the third party requester in the request for reexamination at p. 95, line 22-p. 101, line 16 and claim chart-J.6., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 16. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Palzkill.

This rejection was proposed by the third party requester in the request for reexamination at p. 101, line 17-p. 107, line 19 and claim chart-J.7., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 17. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Botstein.

This rejection was proposed by the third party requester in the request for reexamination at p. 107, line 20-p. 114, line 2 and claim chart-J.8., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 18. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Mormeneo.

This rejection was proposed by the third party requester in the request for reexamination at p. 114, line 3-p. 120, line 13 and claim chart-J.9., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 19. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Sapolsky I and Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 120, line 14-p. 128, line 5 and claim chart-J.10., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 20. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka I in view of Sapolsky II and Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 128, line 6-p. 135, line 18 and claim chart-J.11., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 21. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 135, line 19-p. 141, line 16 and claim chart-K.1., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 22. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Szybalski.

This rejection was proposed by the third party requester in the request for reexamination at p. 141, line 17-p. 147, line 11 and claim chart-K.2., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 23. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Cease I.

This rejection was proposed by the third party requester in the request for reexamination at p. 147, line 12-p. 153, line 8 and claim chart-K.3., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 24. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Cease II.

This rejection was proposed by the third party requester in the request for reexamination at p. 153, line 9-p. 158, line 22 and claim chart-K.4., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 25. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Dobrynin.

This rejection was proposed by the third party requester in the request for reexamination at p. 159, line 1-p. 164, line 15 and claim chart-K.5., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 26. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Kuznedelov.

This rejection was proposed by the third party requester in the request for reexamination at p. 164, line 16-p. 170, line 8 and claim chart-K.6., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 27. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Palzkill.

This rejection was proposed by the third party requester in the request for reexamination at p. 170, line 9-p. 176, line 8 and claim chart-K.7., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 28. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Botstein.

This rejection was proposed by the third party requester in the request for reexamination at p. 176, line 9-p. 182, line 20 and claim chart-K.8., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 29. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Mormeneo.

This rejection was proposed by the third party requester in the request for reexamination at p. 182, line 21-p. 189, line 6 and claim chart-K.9., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 30. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Sapolsky I and Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. p. 189, line 7-p. 196, line 23 and claim chart-K.10., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 31. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Poustka II in view of Sapolsky II and Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 191, line 1-p. 204, line 13 and claim chart-K.11., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 32. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 204, line 15-p. 210, line 16 and claim chart-L.1., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 33. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Szybalski.

This rejection was proposed by the third party requester in the request for reexamination at p. 210, line 17-p. 216, line 18 and claim chart-L.2., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 34. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Cease I.

This rejection was proposed by the third party requester in the request for reexamination at p. 216, line 19-p. 222, line 22 and claim chart-L.3., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 35. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Cease II.

This rejection was proposed by the third party requester in the request for reexamination at p. 222, line 23-p. 228, line 19 and claim chart-L.4., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 36. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Dobrynin.

This rejection was proposed by the third party requester in the request for reexamination at p. 228, line 20-p. 234, line 17 and claim chart-L.5., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 37. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Kuznedelov.

This rejection was proposed by the third party requester in the request for reexamination at p. 234, line 18-p. 240, line 18 and claim chart-L.6., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 38. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Palzkill.

This rejection was proposed by the third party requester in the request for reexamination at p. 240, line 9-p. 246, line 22 and claim chart-L.7., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 39. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Botstein.

This rejection was proposed by the third party requester in the request for reexamination at p. 246, line 23-p. 253, line 8 and claim chart-L.8., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 40. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Mormeneo.

This rejection was proposed by the third party requester in the request for reexamination at p. 253, line 9-p. 259, line 21 and claim chart-L.9., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 41. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 260, line 1-p. 265, line 23 and claim chart-M.1., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 42. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Szybalski.

This rejection was proposed by the third party requester in the request for reexamination at p. 266, line 1-p. 271, line 21 and claim chart-M.2., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 43. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Cease I.

This rejection was proposed by the third party requester in the request for reexamination at p. 271, line 22-p. 277, line 16 and claim chart-M.3., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 44. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Cease II.

This rejection was proposed by the third party requester in the request for reexamination at p. 277, line 17-p. 283, line 6 and claim chart-M.4., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 45. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Dobrynin.

This rejection was proposed by the third party requester in the request for reexamination at p. 283, line 7-p. 288, line 19 and claim chart-M.5., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 46. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Kuznedelov.

This rejection was proposed by the third party requester in the request for reexamination at p. 288, line 20-p. 294, line 16 and claim chart-M.6., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 47. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Palzkill.

This rejection was proposed by the third party requester in the request for reexamination at p. 294, line 17-p. 300, line 21 and claim chart-M.7., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 48. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky II in view of Botstein.

This rejection was proposed by the third party requester in the request for reexamination at p. 300, line 22-p. 306, line 22 and claim chart-M.8., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 49. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Sapolsky I in view of Mormeneo.

This rejection was proposed by the third party requester in the request for reexamination at p. 307, line 1-p. 313, line 6 and claim chart-M.9., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 50. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Mandecki.

This rejection was proposed by the third party requester in the request for reexamination at p. 313, line 9-p. 319, line 11 and claim chart-N.1., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 51. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Szybalski.

This rejection was proposed by the third party requester in the request for reexamination at p. 319, line 12-p. 325, line 7 and claim chart-N.2., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 52. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Cease I.

This rejection was proposed by the third party requester in the request for reexamination at p. 325, line 8-p. 331, line 2 and claim chart-N.3., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 53. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Cease II.

This rejection was proposed by the third party requester in the request for reexamination at p. 331, line 3-p. 336, line 21 and claim chart-N.4., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 54. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Dobrynin.

This rejection was proposed by the third party requester in the request for reexamination at p. 336, line 22-p. 342, line 9 and claim chart-N.5., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 55. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Kuznedelov.

This rejection was proposed by the third party requester in the request for reexamination at p. 342, line 10-p. 348, line 2 and claim chart-N.6., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 56. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Pałzkill.

This rejection was proposed by the third party requester in the request for reexamination at p. 348, line 3-p. 354, line 3 and claim chart-N.7., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 57. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Botstein.

This rejection was proposed by the third party requester in the request for reexamination at p. 354, line 4-p. 360, line 11 and claim chart-N.8., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Ground 58. Claims 1-5 are rejected under 35 USC 103(a) as being unpatentable over Velculescu in view of Mormeneo.

This rejection was proposed by the third party requester in the request for reexamination at p. 360, line 12-p. 366, line 18 and claim chart-N.9., which statements are incorporated herein by reference for the grounds of rejection. It is adopted as set forth.

Status of Claims

4. Claims 1-5 are rejected.

Papers To Be Submitted in Response to Action

5. In order to ensure full consideration of any amendments, affidavits or declarations, or other documents as evidence of patentability, such documents must be submitted in response to this Office action. Submissions after the next Office action, which is intended to be an Action Closing Prosecution (ACP), will be governed by 37 CFR 1.116(b) and (d), which will be strictly enforced.

Extensions of Time

6. Extensions of time under 37 CFR 1.136(a) will not be permitted in inter partes reexamination proceedings because the provisions of 37 CFR 1.136 apply only to "an applicant and not to the patent owner in a reexamination proceeding. Additionally, 35 U.S.C. 314(c) requires that inter partes reexamination proceedings "will be conducted with special dispatch (37 CFR 1.937). Patent owner extensions of time in inter partes reexamination proceedings are provided for in 37 CFR 1.956. Extensions of time are not available for third party requester comments, because a comment period of 30 days from service of patent owner's response is set by statute. 35 U.S.C. 314(b)(3).

Duty to Disclose

7. The patent owner is reminded of the continuing responsibility under 37 CFR 1.985(a), to apprise the Office of any litigation activity, or other prior or concurrent proceeding, involving Patent No. 7,598,035 throughout the course of this reexamination proceeding. The third party requester is also reminded of the ability to similarly apprise the Office of any such activity or proceeding throughout the course of this reexamination proceeding.

Inter Partes Service of Papers

8. After the filing of a request for reexamination by a third party requester, any document filed by either the patent owner or the third party requester must be served on the other party (or parties where two or more third party requester proceedings are merged) in the reexamination proceeding in the manner provided in 37 CFR 1.248. See 37 CFR 1.903.

Amendment in Reexamination Proceedings

9. Patent owner is notified that any proposed amendment to the specification and/or claims in this reexamination proceeding must comply with 37 CFR 1.530(d)-(j), must be formally presented pursuant to 37 CFR 1.52(a) and (b), and must contain any fees required by 37 CFR 1.20(c).

Future Correspondence

10. All correspondence relating to this *inter partes* reexamination proceeding should be directed as follows:

By EFS: Registered users may submit via the electronic filing system EFS-Web at https://sportal.uspto.gov/authenticate/authenticateuserlocalepf.html

By U.S. Postal Service Mail to:

Mail Stop *Inter Partes* Reexam
ATTN: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

By FAX to: (571) 273-9900
Central Reexamination Unit

By hand to: Customer Service Window
Randolph Building
401 Dulany St.
Alexandria, VA 22314

/Sharon Turner/
Primary Examiner, CRU-3991

Conferee: /Bruce Campell/
Primary Examiner, CRU-3991

Conferee:

DEBORAH D. JONES
CRU SPE-AU 3991

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	10962337
Filing Date	2004-10-08
First Named Inventor	Macevicz, Stephen C.
Art Unit	
Examiner Name	
Attorney Docket Number	

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
/ST/	1	5827704		1998-10-27	CEASE et al.	
/ST/	2	5710000		1998-01-20	SAPOLSKY et al.	
/ST/	3	5677153		1997-10-14	BOTSTEIN et al.	

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10962337
	Filing Date	2004-10-08
	First Named Inventor	Macevicz, Stephen C.
	Art Unit	
	Examiner Name	
	Attorney Docket Number	

If you wish to add additional Foreign Patent Document citation information please click the Add button

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, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
/ST/	1	CEASE and LOHFF, A Vector for Facile PCR Product Cloning and Modification Generating Any Desired 4-Base 5' Overhang: pRPM, BioTechniques, 1993, pp. 250-255, Vol. 14, No. 2, USA.	☐
/ST/	2	DOBRYNIN et al., Plasmid Vectors pBBV for Cloning and Regeneration of DNA Fragments with Any End Nucleotide Sequence, Reports of the USSR Academy of Sciences, 1984, pp. 1001-1006, Vol. 278, No. 4, USSR.	☒
/ST/	3	KUZNEDELOV et al., Plasmid Vector pSSCI for Cloning Synthetic Polynucleotides and Their Regeneration with A Unique Terminal Nucleotide Sequence, Bioorganic Chemistry,1986, pp. 842-845, Vol. 12, No. 6, USSR.	☒
/ST/	4	MANDECKI and BOLLING, FokI method of gene synthesis, Gene, 1988, pp. 101-107, Vol. 68, USA.	☐
/ST/	5	MORMENEO et al., Precise nucleotide sequence modifications with bidirectionally cleaving class-IIS excision linkers, Gene, 1987, pp. 21-30, Vol. 61, USA.	☐
/ST/	6	PALZKILL and BOTSTEIN, Probing B-Lactamase Structure and Function Using Random Replacement Mutagenesis, Proteins: Structure, Function, and Genetics, 1992, pp. 29-44, Vol. 14, USA.	☐
/ST/	7	POUSTKA and LEHRACH, Jumping libraries and linking libraries: the next generation of molecular tools in mammalian genetics, TIG, July 1986, pp. 174-179, Amsterdam.	☐
/ST/	8	POUSTKA et al., Construction and use of human chromosome jumping libraries from NotI-digested DNA, Nature, 1987, pp. 353-355, Vol. 325, USA.	☐
/ST/	9	SAPOLSKY and LIPSHUTZ, Mapping Genomic Library Clones Using Oligonucleotide Arrays, Genomics, 1996, pp. 445-456, Vol. 33, USA.	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	10962337
	Filing Date	2004-10-08
	First Named Inventor	Macevicz, Stephen C.
	Art Unit	
	Examiner Name	
	Attorney Docket Number	

/ST/	10	SZYBALSKI et al., Class-IIS restriction enzymes - a review, Gene, 1991, pp. 13-26, Vol. 100, USA.	☐
/ST/	11	VELCULESCU et al., Serial Analysis of Gene Expression, Science, October 20, 1995, pp. 484-487, Vol. 270, USA.	☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/Sharon Turner/	Date Considered	02/08/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.