IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Ex Parte Reexamination of:	)	
	)	
LEDER, PHILIP et al.	)	
	)	**Confirmation No. TBD**
U.S. Patent No.: 5,925,803	)	
Filed: Sept. 19, 1991	)	**Examiner: TBD**
Issue Date*:* July 20, 1999	)	
	)	**Group Art Unit: TBD**
For: TESTING METHOD USING	)	
TRANSGENIC MICE EXPRESSING	)	
AN ONCOGENE	)	
	)	
	)	

REQUEST FOR *EX PARTE* REEXAMINATION

Mail Stop *Ex Parte* Reexam
Central Reexamination Unit
Office of Patent Legal Administration
United States Patent & Trademark Office
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Alexandria, VA 22313-1450

The Third Party Requestor (TPR) requests that the USPTO reexamine United States Patent No. 5,925,803 (the "'803 Patent"; provided at Appendix 1) because of the substantial new questions of patentability (SNQ) provided herein.

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I. INTRODUCTION

TPR respectfully requests a Reexamination proceeding be instituted for the three claims of U.S. Patent 5,925,803 (the '803 Subject Patent). The '803 Subject Patent claims methods for screening compounds using transgenic animals. A Grandparent Patent, US Pat. 7,736,866 ('866 Grandparent Patent) claims the transgenic animals themselves and is now expired. The record demonstrates that the '803 Subject Patent is also expired. Further, the claims of the '803 Subject Patent are not patentable in view of obviousness-type double patenting -- in short, screening compounds using the animals of the expired '866 Grandparent Patent is obvious and cannot merit a second patent that extends the monopoly of the '866 for an additional 11 years. Additionally, the claims are obvious in view of the art under 35 U.S.C. 103(a), as the art taught the transgenic animals as claimed and taught use of such animals for screening compounds. This is particularly true in light of modern obviousness case law, such as the Supreme Court holding in *KSR Int'l Co. v. Teleflex Inc*.

First, a Reexamination is necessitated in that the '803 Subject Patent claims are not patentable under obviousness-type double patenting over the claims of the '866 Grandparent Patent in view of Ward et al. or Schach et al. During prosecution of the '803 Subject Patent, when the Patentee was faced with a *defacto* obviousness-type double patenting rejection over the '866 Grandparent Patent in view of Ward et al. or Schach et al., they were successful in having this rejection withdrawn by asserting that such a rejection was legally improper *because* the application was a divisional application. As the '803 Subject Patent is not a divisional application, the obviousness rejection was not properly traversed and therefore raises a first substantial new question of patentability (SNQ).

Second, a Reexamination is necessitated in that the '803 Subject Patent claims are not patentable under obviousness-type double patenting (ODP) over Claims 1-12 of the '866 Grandparent Patent as they are not patentably distinct. During prosecution of U.S. Pat. 5,087,571 (the '571 Parent Patent), claims corresponding to those that issued in the '803 Subject Patent were rejected under ODP by Examiner Tanenholtz. The Patentee avoided this rejection by filing a terminal disclaimer over the '866 Grandparent Patent and eventually cancelling these corresponding claims in view of enablement rejections. When these same claims were re-presented in the '803 Subject Patent prosecution, Examiner Chambers did not reject the claims under ODP over Claims 1-12 of the '866 Grandparent Patent, perhaps under the belief that a terminal disclaimer was in operation. Regardless of Examiner Chamber's thinking, a substantial new question of patentability exists.

Third, a Reexamination is necessitated in that the '803 Subject Patent claims are not patentable under ODP over the '866 Grandparent Patent claims in view of the Proctor patent, which raises a third SNQ.

Fourth, a Reexamination is necessitated in that the '803 Subject Patent claims are obvious under 35 U.S.C. 103(a) over Schwab et al. As discussed below, during the prosecution of both the '866 Grandparent Patent and '571 Parent Patent, claims corresponding to those that issued in the '803 Subject Patent were rejected as obvious over Schwab et al. by Examiner Tanenholtz. The Patentee avoided these rejections each time by cancelling these corresponding claims. When these same claims were re-presented in the '803 Subject Patent prosecution, this reference was not addressed.

Fifth, a Reexamination is necessitated in that the '803 Subject Patent claims are obvious under 35 U.S.C. 103(a) over Jaenisch et al. in view of the Proctor patent, which raises a fifth SNQ.

Sixth, a Reexamination is necessitated in that the '803 Subject Patent claims are obvious under 35 U.S.C. 103(a) over Jaenisch et al. in view of the either Ward et al. or Schach et al., which raises a sixth SNQ.

II. REEXAMINATION OF THE '803 SUBJECT PATENT IS PROPER

Prior to discussing the issues involved with this Reexamination Request, TPR respectfully notes that Reexamination is properly declared even though: 1) the '803 Subject Patent is expired; and 2) a number of the bases for the request involve obviousness type double-patenting.

As explained in more detail below, the '803 Subject Patent expired on July 12, 2005 because the immediate parent application ('571 Parent Patent) contains a terminal disclaimer over the '866 Grandparent Patent that disclaims any term of the '571 Parent Patent *and any downstream applications* (which includes the '803 Subject Patent) that would extend beyond the July 12, 2005 expiration date of the '866 Grandparent Patent. Even though the '803 Subject Patent is expired, Reexamination is still properly declared. In particular, under MPEP 2211, a Reexamination may be declared for an expired patent at any time during the *enforceability* of the patent. The enforceability of a patent extends six years past the expiration date (*see, e.g.*, MPEP 2211). As the '803 Subject Patent expired on July 12, 2005, its period of enforceability (e.g., for damages that occurred up until July 12, 2005) runs until July 12, 2011, thereby making it currently eligible for Reexamination.

It is also important to note that obviousness type double-patenting is a proper basis upon which to declare a Reexamination. As noted in MPEP 2217:

> Typically, substantial new questions of patentability in a reexamination proceeding are based on "prior art" patents and publications. There are exceptions, however. For example, in *In re Lonardo*, 119 F.3d 960, 43 USPQ2d 1262 (Fed. Cir. 1997), the Federal Circuit upheld a nonstatutory double patenting rejection in which the patent upon which the rejection was based and the patent under reexamination shared the same effective filing date.

As such, in this case, Reexamination of the '803 Subject Patent is properly declared based on the described obviousness-type double patenting rejections, even if the Patent Office determines that the 103(a) obviousness rejections described herein do not raise a substantial new question of patentability.

Finally, even if the Patent Office determines that: 1) the 103(a) obviousness rejections proposed herein do not raise a substantial new question of patentability; and 2) the terminal disclaimer in the '571 parent application insulates the '803 Subject Patent from any double patenting rejection; TPR respectfully requests that a Reexamination nonetheless be declared to serve the public notice function of Reexaminations (i.e., to make it clear on the record that the '803 Subject Patent is only avoiding the double-patenting rejections *because* of the terminal disclaimer in the '571 Parent Patent, which likewise informs the public that the patent expired on July 12, 2005). In such a case, even if a Reexamination is not declared, to serve the public notice function, TPR respectfully requests that the Patent Office indicate in writing that the terminal disclaimer in the '571 Parent Patent application insulates the '803 Subject Patent from obviousness type double patenting rejections, and further, affirmatively state that the '803 Subject Patent therefore expired on July 12, 2005. This public notice function is particularly important in this case as the Patentee is publicly advertising that the '803 Subject Patent does not expire until July of 2016, which is 11 years past the actual expiration date. Evidence of the Patentee's public claims that the '803 Subject Patent does not expire until July of 2016 is provided at Appendix 2 (Dupont Web site print out; see "Frequently Asked Questions) and Appendix 3 (publicly available Dupont + Univ. of Pittsburgh license; see Attachment A).

III. CLAIMS FOR WHICH REEXAMINATION IS REQUESTED, PRIOR ART, AND SNQs

A. Reexamination Is Requested For All Claims (1-3) of the '803 Patent

Requester submits that substantial new questions of patentability exist as to Claims 1-3 of the '803 Subject Patent and requests *ex parte* reexamination of these claims based on the questions of patentability presented below.

B. Listing of the Prior Art Upon Which Reexamination is Requested

i. Claims 1-12 of U.S. Patent 4,736,866 (Appendix 4)
ii. Ward et al., Toxicol., Appl. Pharmacol., 51:389-397 (1979) (Appendix 5)
iii. Schach et al., Fund. Appl. Toxicol., 3:631-639 (1983) (Appendix 6)
iv. Schwab et al, EPA-600/9-82-013, Sym: Carcinogen, Polynucl. Aromat. Hydrocarbons Mar. Environ., 212-32 (1982). (Appendix 7)
v. U.S. Patent 4,360,510 to Proctor ("Proctor Patent," Appendix 11)
vi. Jaenisch et al., PNAS, USA, 71(4):1250-1254 (1974) (Appendix 12).

C. Summary of Substantial New Questions of Patentability

SNQ1: Claim 1 of the ‘803 Subject Patent is obvious in view of Claims 1, 11, and 12 of the '866 Grandparent Patent in view of Ward et al. or Schach et al. under the doctrine of judicially created obviousness-type double patenting.

SNQ2: Claims 1-3 of the ‘803 Subject Patent are unpatentable in view of the Claims 1-12 of the '866 Grandparent Patent under the doctrine of judicially-created obviousness-type double patenting.

SNQ3: Claims 2-3 of the ‘803 Subject Patent are obvious in view of the claims of the '866 Grandparent Patent in view of the Proctor Patent, under the doctrine of judicially-created obviousness-type double patenting.

SNQ4: Claims 1-3 of the ‘803 Subject Patent are obvious under 35 U.S.C. 103(a) in view of Schwab et al.

SNQ5: Claims 2-3 of the ‘803 Subject Patent are obvious under 35 U.S.C. 103(a) over Jaenisch et al. in view of the Proctor patent.

SNQ6: Claim 1 of the ‘803 Subject Patent is obvious under 35 U.S.C. 103(a) over Jaenisch et al. in view of the either Ward et al. or Schach et al.

IV. SUMMARY OF THE PROSECUTION OF THE '866, '571 AND '803 PATENTS

a. The '866 Patent ("'866 Grandparent Patent")

i. On June 22, 1984, the President and Fellows of Harvard College filed U.S. Application No. 06/623,774 (the '"774 Application") drawn to the inventions of Philip Leder and Timothy Stewart.

ii. Originally-filed claims 1-22[1] can be summarized as follows:
   1. Claims 1-12 were drawn to transgenic animals containing a human oncogene;
   2. Claims 13-19 were drawn to methods of testing a material suspected of being a carcinogen using the transgenic animals; methods of culturing cells from the transgenic animals; and methods of testing compounds which are suspected of conferring protection against the development of neoplasms using the transgenic animals;[2] and
   3. Claims 20-22 were drawn to specific plasmid constructs.

iii. The USPTO issued a Non-Final Office Action on November 3, 1986 rejecting all of claims 1-24:
   1. Claims 1-10 and 13-19 were rejected under 35 U.S.C. 112, first paragraph as not being supported by an enabling disclosure for their entire scope;
   2. Claims 20-22 were rejected under 35 USC 112, second paragraph as being indefinite;
   3. Claims 1-12 were rejected under 35 USC 101 as being drawn to non-statutory subject matter;
   4. Claims 1-24 were rejected as being obvious under 35 USC 103 Ellis, Goldfarb, Huang, Blair, Der, Shih, Gorman, Weinberg in view of any one of Wagner, Palmiter (Cell), Palmiter (Patent) and Constantini in further view of Schwab;
   5. Claims 1-3 and 10 were rejected as either anticipated under 35 USC 102(b) or, in the alternative, obvious under 35 USC 103 over Schwab;
   6. Claims 13 and 15-19 were rejected as obvious under 35 USC 103 over Schwab;
   7. Claim 14 was rejected as being obvious under 35 USC 103 over Ucker and Goldfarb; and

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[1] Originally-filed claims in '866 patent (Appendix 10)

[2] It bears noting that claim 1 of the '803 Patent corresponds to original claim 13 of the '866 patent; and claims 2 and 3 are substantially similar to original claims 18 and 19 of the '866 Grandparent Patent.

8. Claims 20-24 were rejected as being anticipated under 35 USC 102(b) by Ellis, Goldfarb, Huang, Blair, Der, Shih, Gorman, Weinberg.

iv. On May 1, 1987, the Applicants responded by amending claims to replace "animal" with the term "mammal" in claims 1 -15, 18, and 19 and inserted ATCC deposit numbers in claims 20-24. The Applicant continued to prosecute all 24 claims by submitting a declaration of Philip Leder with accompanying arguments rebutting the rejections of record.

v. On July 31, 1987, the USPTO issued a Final Rejection of claims 1-24:
   1. Claims 1-12 were held to be free of the prior art but objected to because the specification was non-enabling for the oncogene recombinant plasmids;
   2. Claims 13, 15-19 were rejected as obvious under 35 USC 103 over Schwab;
   3. Claim 14 was rejected as being obvious under 35 USC 103 over Ucker and Goldfarb; and
   4. Claims 20-24 were rejected as being anticipated under 35 USC 102(b) by, or in the alternative obvious under 35 USC 103 over, Ellis, Goldfarb, Huang, Blair, Der, Shih, Gorman, and Weinberg.

vi. On September 9, 1987, the Applicants filed a Response After Final Rejection cancelling claims 13-24.

vii. On December 15, 1987, the USPTO issued an Advisory Action regarding the lack of evidence with regard to the ATCC deposits.

viii. The Applicants then corrected the defect by submitting Declarations of Availability regarding the ATCC deposited recombinant plasmids.

ix. On February 1, 1988, the USPTO issued a Notice of Allowance for claims 1-12.

x. On April 12, 1988, the USPTO issued the'774 Application as the '866 Patent.

b. The '571 Patent ("'571 Parent Patent")

i. On March 22, 1988, the President and Fellows of Harvard College filed U.S. Application No. 07/171,806 (the '"806 Application") as a Divisional application of the parent '774 Application ('866 Patent) with a preliminary amendment cancelling claims 1-12.[3]

ii. On November 14, 1985, the USPTO issued a Non-Final Office Action rejecting claims 13-24[4]:

[3] It bears noting that this application was filed as a divisional application despite the absence of a Restriction Requirement during the prosecution of the '866 Grandparent Patent.

[4] Primary Examiner Tanenholtz, the same examiner of the '866 Grandparent patent, penned this Non-Final Office Action.

1. Claims 13-19 were rejected as not being enabled for their full scope under 35 USC 112, first paragraph and Claims 13, 14, 18 and 19 under the second paragraph as being dependent upon canceled claims;
2. Claims 13, 18 and 19 were rejected under the judicially-created doctrine of obviousness double patenting as being unpatentable over claims 1-12 of the '866 Patent;
3. Claim 14 was rejected as being obvious under 35 USC 103 over Ucker and Goldfarb;
4. Claims 15-17 were rejected as obvious under 35 USC 103 over Wagner, Palmiter and Constantini;
5. Claims 13, 18 and 19 were rejected as being obvious under 35 USC 103 over Schwab; and
6. Claims 20-24 were rejected as being anticipated under 35 USC 102(b) by, or in the alternative obvious under 35 USC 103 over, Ellis, Goldfarb, Huang, Blair, Der, Shih, Gorman, and Weinberg.

iii. On June 20, 1989, the USPTO issued a Notice of Abandonment for failure to respond to the November 14, 1988 Non-Final Office Action.

iv. On November 16, 1989, six months after the mailing of Notice of Abandonment, the Applicants filed a Petition to Revive accompanied by a Response, Amendments to the claims, a declaration by Philip Leder and a Terminal Disclaimer. A summary of these documents follow:

7. Applicants' Response included amendments to claims 13-19 to address in part the 112 and 103 rejections of record, cancelation of claims 20-24 to address the 102(b) rejection of record and added claim 25 drawn to a somatic cell derived from the transgenic animals;
8. Applicants' Response addressed the obviousness-type double patenting rejection over the parent '866 Patent by providing a terminal disclaimer that includes the following language: [5]

> Your petitioner, President and Fellows of Harvard College, hereby disclaims any portion of any patent granted on the above-identified application or on any application which is entitled to the benefit of the filing date of this application under 35 U.S.C. §120 not extending the term of any patent granted on that application beyond the term of issued U.S. Patent No. 4,736,866 issued April 12, 1988. This agreement is

[5] See Terminal Disclaimer from '571 Parent Patent (Ser. No. 07/171,806) at Appendix 9.

9. The Applicants' Response also included the Declaration of Dr. Philip Leder that was submitted during the parent '774 Application in support of non-obviousness of claims 15-17.

v. On June 20, 1990, the USPTO issued a second Non-Final Office Action rejecting claims 13-19 and 25 under 35 USC 112, first paragraph as not being enabled for all mammals and not being enabled for all oncogenes.[6]

vi. On December 18, 1990, the Applicants submitted a Response presenting arguments based upon scientific literature in attempts to overcome the rejections of record.

vii. On February 25, 1991, the USPTO issued a Final Office Action maintaining the rejections of the June 1990 Non-Final Office Action.

viii. On June 25, 1991, the Applicants submitted a Response cancelling claims 15-17 and amending claim 25 to include "non-human" (per a suggestion by the Examiner) to obviate a 112, second paragraph rejection. In addition, the Response continued to argue the enablement rejections pointing to the issued claims of the '866 Patent, which include all mammals and all oncogenes, as proof that the disclosure in the present application was enabled for all mammals and for all oncogenes.

ix. On July 15, 1991, the USPTO issued an Advisory Action that indicated that claims 14 and 25 were allowable and that claims 13, 18 and 19 remained rejected.

x. On August 9, 1991, the Applicants filed a Response cancelling claims 13, 18 and 19.

xi. On August 26, 1991, the USTPO issued a Notice of Allowance with an Examiner's Amendment to claim 25.

xii. On February 11, 1992, the USPTO issued the'806 Application as the '571 Patent.

c. The '803 Patent ("'803 Subject Patent")

i. On August 27, 1991, the President and Fellows of Harvard College filed U.S. Application No. 07/750,510 (the "'510 Application") as a continuation application of the '806 Application (the '571 Patent) with the originally-filed claims 1-13 and 15-24 of the '774 Application (the '866 Patent).

ii. On August 31, 1992, the USPTO issued a Restriction Requirement dividing the claims into three groups: i) Group I – Claims 1-12 and 15-17 being drawn

[6] Examiner Jasmine C. Chambers, Ph.D wrote this Office Action.

to a transgenic animal and method of making the same; ii) Group II – Claims 13, 18 and 19 being drawn to methods of testing materials suspected of being a carcinogen and methods of testing materials suspected of having a protective effect against the development of neoplasms using the transgenic animals; and iii) claims 20-24 drawn to plasmids.

iii. On September 23, 1992, the Applicants elected Group II, claims 13, 18 and 19.

iv. On December 11, 1992, the USPTO issued a Non-Final Office Action (i) withdrawing claims 1-12, 15-17 and 20-24 and (ii) rejecting claims 13, 18 and 19 as not being enabled for all mammals and all oncogenes.

v. On June 11, 1993, Applicants submitted a Response with amendments to claims 13, 18 and 19 as well as arguments to obviate the enablement rejections of record based largely upon 16 post-filing scientific references related to various transgenic animals carrying a variety of oncogenes.

vi. On November 2, 1993, the USPTO issued a Non-Final Office Action maintaining the enablement rejections under 35 USC 112, first paragraph as well as introducing a new rejection that claims 13, 18 and 19 are obvious under 35 USC 103 over Ward or Schah. The obviousness rejection relies upon the precedent of *In re Durden*, 763 F.2d 1406, 226 USPQ 359 (Fed. Cir. 1985) and *In re Albertson,* 332 F.2d 379, 141 USPQ 730 (CCPA 1964) standing for the proposition that when the materials are novel, the application of old methods or processes using the novel materials to produce an expected result would be obvious.

vii. On February 18, 1994, the Applicants submitted a Response reiterating their arguments against the outstanding scope of enablement rejection with an emphasis on the post-filing data and in view of the breadth of the claims that issued in the '866 Patent. In addition, the Applicants argued that the Examiner improperly combined the teaching in the prior issued '866 Patent with Ward and Schah to reject the claims as obvious because 35 USC 121 prohibits the USPTO from rejecting a later divisional application,

> where (as here) the divisional application is filed as a result of a restriction requirement in the original case…[T]he Examiner has used Applicants' own teaching concerning the novel and non-obvious oncomice claimed in U.S. Patent No. 4,736,866 (a predecessor to the present case) as though it were prior art, in order to make the

claims to methods of using the oncomice appear to be obvious.[7]

viii. On May 5, 1994, the USPTO issued a Final Office Action rejected claims 13, 18 and 19 maintaining both the scope of enablement rejections as well as the obviousness rejection over Ward and Schah.

ix. On June 26, 1994, the Applicants filed a response reiterating their enablement and non-obviousness arguments in more detail, this time walking through the *Wands* factors to argue enablement. In addition, the Applicants filed a Notice of Appeal.

x. On August 26, 1994, the USPTO issued an Advisory Action maintaining the rejections of record.

xi. On September 26, 1994, Applicants filed an Appeal Brief reiterating in large part the arguments that they had provided in their past responses.

xii. On January 9, 1995, the USPTO issued an Examiner's Answer, wherein the Examiner withdrew the obviousness rejection of record and provided a post filing reference in support of the Examiner's scope of enablement rejection.

xiii. On March 9, 1995, the Applicants submitted their Reply Brief and provided two additional post-filing references to rebut the Examiner's arguments presented in the Examiner's Answer.

xiv. On June 27, 1995, the USPTO issued a communication indicating that Applicants' Reply Brief was improper because no new issues were raised in the Examiner's Answer and that the Reply Brief was not entered.

xv. On September 29, 1997, Applicants submitted a Status Inquiry.

xvi. On May 27, 1998, the Board of Appeals issued an opinion that simply remanded the case to the Examiner.

xvii. On November 19, 1998, the USPTO issued a Notice of Allowance of all claims along with an Examiner's Amendment.

xviii. On July 20, 1999, the USPTO issued U.S. Patent No. 5,925,803.

[7] It bears noting that no Restriction Requirement appeared in the '866 Grandparent Patent and the '803 patent was filed as a continuing application, not a divisional.

V. THE '803 SUBJECT PATENT EXPIRED JULY 12, 2005 VIA A TERMINAL DISCLAIMER WHICH CANNOT BE NULLIFIED BY THE PATENTEE

A. The '803 Subject Patent Expired On July 12, 2005

The determination of whether or not a patent has expired at the outset of a re-examination is a threshold issue because different rules and procedures apply to the reexamination of an expired patent. For example, the claims of an expired patent cannot be amended during a reexamination proceeding and the USPTO applies a different claim interpretation standard as a result.[8] As such, it is important to determine if the '803 Subject Patent is expired or not.

In the '571 Parent Patent, the Patentee filed a terminal disclaimer which not only disclaimed the term of the '571 Parent Patent back to the term of the '866 Grandparent Patent (which expired on July 12, 2005), but also disclaimed the term of any subsequent patents claiming priority to the '571 Parent Patent - which includes the subject '803 Subject Patent. This terminal disclaimer is provided at Appendix 9, with the relevant language presented below:

> Your petitioner, President and Fellows of Harvard College, hereby disclaims any portion of any patent granted on the above-identified application or on any application which is entitled to the benefit of the filing date of this application under 35 U.S.C. §120 not extending the term of any patent granted on that application beyond the term of issued U.S. Patent No. 4,736,866 issued April 12, 1988.

[8] *See* MPEP § 2258 (I) (G): "In a reexamination proceeding involving claims of an expired patent, claim construction pursuant to the principle set forth by the court in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316, 75 USPQ2d 1321, 1329 (Fed. Cir. 2005) (words of a claim "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art in question at the time of the invention) should be applied since the expired claim are not subject to amendment."

The TPR submits that in view of the language of the Terminal Disclaimer (disclaiming "any application which is entitled to the benefit of the filing date of this application") the '803 Subject Patent is terminally disclaimed over the '866 Grandparent Patent and therefore expired on July 12, 2005. In other words, it is submitted that the Assignee completed an agreement with the public that not only the '571 Parent Patent would terminate on the same date as the '866 Grandparent Patent, but also any further applications that claimed priority benefit to the '571 Parent Patent would also expire on the same date - which includes the '803 Subject Patent.

It is noted that in some terminal disclaimers, the language regarding downstream applications does not exist because the Applicant only wishes to have the terminal disclaimer affect the term of the current application which has been rejected based upon obviousness-type double patenting (ODP), not all other later applications claiming benefit to the current application.[9] The model terminal disclaimer language provided by the MPEP includes the following:

> The owner, _____, of _____ percent interest in the instant application hereby disclaims the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **reference patent** No. _____ as the term of said prior patent is defined in **35 U.S.C. 154** and **173** , and as the term of said **reference patent** is presently shortened by any terminal disclaimer.[10]

The language in the terminal disclaimer from the '571 Parent Patent deviates from the standard terminal disclaimer by disclaiming the term of all downstream patents. However, such language is permitted and contemplated by the MPEP. For example, the MPEP specifically addresses whether or not a terminal disclaimer in a parent application carries forward to affect subsequent continuing applications. MPEP 1490 (V)(B) provides:

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[9] *See* MPEP 1490

[10] *See Id.*

> "[a] terminal disclaimer filed to obviate a nonstatutory double patenting rejection is effective only with respect to the application identified in the disclaimer ***unless by its terms it extends to continuing applications***." (emphasis added) [11]

In this case, by its terms, the terminal disclaimer filed in the '571 Parent Patent extends to the '803 Subject Patent (as contemplated by MPEP 1490 (V)(B)), and therefore, the '803 Subject Patent expired on the same day as the '866 Grandparent Patent and the '571 Parent Patent (i.e., expired on July 12, 2005).

The MPEP makes clear that there is no *per se* protection of continuing applications against the effects of terminal disclaimers filed in a parent application and that the terms of the terminal disclaimer control.[12] TPR submits that the Assignee entered into an agreement with the USPTO and with the public stating that no other patent emanating from any application claiming priority to the '571 Parent Patent would be enforceable beyond July 12, 2005, therefore, the '803 Subject Patent has been expired for nearly 5 years. To the extent that the Patentee argues that the language of the terminal disclaimer does not reach the '803 Subject Patent, which is a continuing application claiming priority benefit under 120, the Patent Office should strongly construe the terminal disclaimer language against the Patentee as the drafter as it would in any other contract interpretation dispute.[13] The equities would demand such and interpretation in the present case, where the other party to the agreement is the public. Moreover, even if the Patent Office were to determine that the terminal disclaimer does not necessarily apply to *all* subsequent continuations (despite its clear language to the contrary) the disclaimer should certainly apply to the '803 Subject Patent, because the claims that ultimately issued in the '803 Subject Patent are nearly identical to claims that were pending in the '571 Parent Patent at the time the Terminal Disclaimer was filed. Thus, the Patentee unequivocally disclaimed additional term for claims directed to the subject matter of the '803 Subject Patent. TPR also submits that since the '803 Subject Patent has expired that the Patentee should not be able to amend the claims of the '803 Subject Patent to address rejections in this reexamination proceeding upon granting of this request.

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[11] MPEP 1490 (V) (B)

[12] *See Id.*

[13] See UNITED STATES v. SECKINGER, 397 U.S. 203 (1970)

B. The Patentee Cannot Nullify the Terminal Disclaimer in Any Reexamination Proceeding or Any Other Type of Corrective Proceeding

Under the law, the Patentee is not permitted to nullify the effect of the terminal disclaimer filed in the '571 Parent Patent on the '803 Subject Patent in any Reexamination that is declared, or by other corrective measures such as Reissue or via a Certificate of Correction. The relevant law is well summarized in MPEP 1490 (VII) "Withdrawing a Recorded Terminal Disclaimer." In particular, part B of this section entitled "After Issuance of a Patent," provides a summary of the law regarding the prohibition against nullifying the effect of a terminal disclaimer in an issued patent. The pertinent text from MPEP 1490 (VII) (B) is provided below:

> B. After Issuance Of Patent
>
> The mechanisms to correct a patent - Certificate of Correction (35 U.S.C. 255), reissue (35 U.S.C. 251), and reexamination (35 U.S.C. 305) - are not available to withdraw or otherwise nullify the effect of a recorded terminal disclaimer. As a general principle, public policy does not favor the restoration to the patent owner of something that has been freely dedicated to the public, particularly where the public interest is not protected in some manner - e.g., intervening rights in the case of a reissue patent. *See, e.g., Altoona Publix Theatres v. American Tri-Ergon Corp.*, 294 U.S. 477, 24 USPQ 308 (1935).
>
> Certificates of Correction (35 U.S.C. 255) are available for the correction of an applicant's mistake. The scope of this remedial provision is limited in two ways - by the nature of the mistake for which correction is sought and the nature of the proposed correction. *In re Arnott*, 19 USPQ2d 1049 (Comm'r Pat. 1991). The nature of the mistake for which correction is sought is limited to those mistakes that are:
>
> (A) of a clerical nature;
>
> (B) of a typographical nature; or
>
> (C) of a minor character.
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> The nature of the proposed correction is limited to those situations where the correction does not involve changes which would:
>
> (A) constitute new matter, or

(B) require reexamination.

A mistake in filing a terminal disclaimer does not fall within any of the categories of mistake for which a certificate of correction of applicant's mistake is permissible, and any attempt to remove or nullify the effect of the terminal disclaimer would typically require reexamination of the circumstances under which it was filed.

Although the remedial nature of reissue (35 U.S.C. 251) is well recognized, reissue is not available to correct all errors. It has been the Office position that reissue is not available to withdraw or otherwise nullify the effect of a terminal disclaimer recorded in an issued patent. First, the reissue statute only authorizes the Director of the USPTO to reissue a patent "for the unexpired part of the term of the original patent." Because ***the granting of a reissue patent without the effect of a recorded terminal disclaimer would result in extending the term of the original patent, reissue under these circumstances would be contrary to the statute***. Second, the principle against recapturing something that has been intentionally dedicated to the public dates back to *Leggett v. Avery*, 101 U.S. 256 (1879). ***The attempt to restore that portion of the patent term that was dedicated to the public to secure the grant of the original patent would be contrary to this recapture principle***. Finally, applicants have the opportunity to challenge the need for a terminal disclaimer during the prosecution of the application that issues as a patent. "Reissue is not a substitute for Patent Office appeal procedures." *Ball Corp. v. United States*, 729 F.2d 1429, 1435, 221 USPQ 289, 293 (Fed. Cir. 1984). Where applicants did not challenge the propriety of the examiner's nonstatutory double patenting rejection, but filed a terminal disclaimer to avoid the rejection, ***the filing of the terminal disclaimer did not constitute error within the meaning of 35 U.S.C. 251***. *Ex parte Anthony*, 230 USPQ 467 (Bd. App. 1982), *aff'd*, No. 84-1357 (Fed. Cir. June 14, 1985).

Finally, the nullification of a recorded terminal disclaimer would not be appropriate in a reexamination proceeding. There is a prohibition (35 U.S.C. 305) against enlarging the scope of a claim during a reexamination proceeding. As noted by the Board in *Anthony*, *supra*, if a terminal disclaimer was nullified, "claims would be able to be sued upon for a longer period than would the claims of the original patent. Therefore, the vertical scope, as opposed to the horizontal scope (where the subject matter is enlarged), would be enlarged." (***emphasis added***).

In light of the law outlined in the MPEP, it is clear that the Patentee cannot be permitted to nullify the effect of the terminal disclaimer filed in the '571 Parent Patent on the term of the '803 Subject Patent.

As such, the '803 Subject Patent expired on July 12, 2005 and this is not subject to change in view of any arguments or procedures that may be put forward by the Patentee.

C. Request for Explicit Statement by the Office Regarding '803 Patent Expiration

TPR respectfully submits that the '803 Subject Patent expired July 12, 2005 and that the Patentee cannot take any corrective action to change this expiration date. As a matter of public notice, TPR respectfully requests that the Patent Office acknowledge these facts in written form - regardless of whether a Reexamination is declared or not. Such a statement by the Patent Office is consistent with Federal Circuit guidance that the claims, specification, *as well as the prosecution history*, should provide the public with notice of what is claimed such that competitors can shape their behavior:

> Public notice of the scope of the right to exclude, as provided by the patent claims, specification and prosecution history, is a critical function of the entire scheme of patent law. The notice function is critical because it provides competitors with the necessary information upon which they can rely to shape their behavior in the marketplace. (*emphasis added, Litton Sys., Inc. v. Honeywell, Inc.,* 145 F.3d 1472, 1474 (Fed. Cir. 1998).

As noted in part II. above, public notice as to the prior expiration of the '803 Subject Patent is of great public importance as the Patentee is currently advertising that the '803 Subject Patent does not expire until July of 2016, which is 11 years past its actual expiration date.[14] As such, even if this Reexamination request is denied, any communication regarding denial of the Reexamination should include the requested statement to provide the public notice as to the status of the '803 Subject Patent.

[14] Evidence of the Patentee's advertising is provided in Appendix 2 (Dupont Web site print out; see "Frequently Asked Questions) and Appendix 3 (publicly available Dupont + Univ. of Pittsburgh license; see Attachment A).

VI. DETAILED DISCUSSION OF SUBSTANTIAL NEW QUESTIONS (SNQs) OF PATENTABILITY

A. Principals of the Law Governing Reexamination

i. Claim Construction Standards for Reexamination

In determining whether a "substantial new question of patentability" has been shown and that reexamination is therefore appropriate, "the PTO must apply the broadest reasonable meaning to the claim language, taking into account any definitions presented in the specification." *In re Bass*, 314 F.3d 575, 577, 65 U.S.P.Q. 1156 (Fed. Cir. 2002) (citing *In re Yamamoto*, 740 F.2d 1569, 1571, 222 U.S.P.Q. 934, 936 (Fed. Cir. 1984)). The requirement that claims be interpreted as broadly as their terms reasonably allow means that the words of the claim must be given their plain meaning unless the applicant has provided a clear definition in the specification. *In re Zietz*, 893 F.2d 319, 321, 13 U.S.P.Q.2d 320, 1322 (Fed. Cir. 1989). The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1360, 49 U.S.P.Q.2d 1464, 1468 (Fed. Cir. 1999).

To the extent the Patent Office agrees that the '803 Subject Patent is expired, then the claims are interpreted as set forth in MPEP § 2258 (I) (G): "In a reexamination proceeding involving claims of an expired patent, claim construction pursuant to the principle set forth by the court in *Phillips v. AWH* Corp., 415 F.3d 1303, 1316, 75 USPQ2d 1321, 1329 (Fed. Cir. 2005) (words of a claim "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art in question at the time of the invention should be applied since the expired claim are not subject to amendment)."

ii. Nonstatutory Obviousness-Type Double Patenting

The law regarding nonstatutory obviousness-type double patenting is summarized in MPEP 804 (II)(B), the pertinent part of which is reproduced below:

> A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). *See,*

> *e.g., In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). In determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is - does any claim in the application define an invention that is anticipated by, or is merely an obvious variation of, an invention claimed in the patent? If the answer is yes, then an "obviousness-type" nonstatutory double patenting rejection may be appropriate. Obviousness- type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent, or a non-commonly owned patent but subject to a joint research agreement as set forth in 35 U.S.C. 103(c)(2) and (3), ***when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent***. *See Eli Lilly & Co. v. Barr Labs., Inc*., 251 F.3d 955, 58 USPQ2d 1869 (Fed. Cir. 2001); *Ex parte Davis*, 56 USPQ2d 1434, 1435-36 (Bd. Pat. App. & Inter. 2000). (***emphasis added***)
>
> A double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

iii. Obviousness Under 35 U.S.C. 103(a)

35 U.S.C. § 103 forbids issuance of a patent when '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. *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 406 (2007). Under 35 U.S.C. § 103, the factual inquiry into obviousness requires a determination of: (1) the scope and content of the prior art; (2) the differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations, if any. *Graham v. John Deere Co*., 383 U.S. 1, 17-18 (1966). As stated in *KSR Int'l Co., v. Teleflex, Inc*., 550 U.S. 398, 418 (2007):

> [A]nalysis [of whether the subject matter of a claim would have been prima facie obvious] need not seek out precise teachings directed to the specific subject matter of the challenged claim,

> for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ. [W]hen a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. at 418 (quoting *Sakraida v. Ag Pro, Inc*., 425 U.S. 273, 282 (1976)).

In *KSR Int'l Co. v. Teleflex Inc*., 127 S.Ct. 1727, 82 U.S.P.Q.2d 1385 (2007), the Supreme Court stressed "the need for caution in granting a patent based on the combination of elements found in the prior art." Id. at 1739. According to the Court, heightened caution is appropriate because "[a] patent for a combination which only unites old elements with no change in their respective functions ... obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Id.

Following *KSR*, the PTO released Examination Guidelines for Determining Obviousness Under 35 US.C 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc*., ("Obviousness Guidelines"), which provide an analysis of the Supreme Court's latest guidance on the question of obviousness.[15] The Obviousness Guidelines delineate a number of concrete rationales for finding an invention obvious (along with the factual underpinnings required for each), which are provided in MPEP § 2141 and 2143, and are reproduced below:

> (A) Combining prior art elements according to known methods to yield predictable results;
>
> (B) Simple substitution of one known element for another to obtain predictable results;
>
> (C) Use of known technique to improve similar devices (methods, or products) in the same way;
>
> (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
>
> (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

[15] 72 Fed. Reg. 57526 (Oct. 10, 2007)

(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

B. SNQ1: Claim 1 Is Unpatentable Under Nonstatutory Obviousness-Type Double Patenting Over Claims 1, 11, and 12 of the '866 Grandparent Patent in View of Either Ward et al. or Schach et al.

The Ward et al. reference was published in 1979, which is more than one year before the earliest filing date (June 22, 1984) of the '803 Subject Patent, and therefore qualifies as prior art under 35 U.S.C. §§ 102(b) and 103(a). The Schach et al. reference was published in November/December of 1983, which is about seven months before earliest filing date (June 22, 1984) of the '803 Subject Patent, and therefore qualifies as prior art under 35 U.S.C. §§ 102(a) and 103(a).[16]

Provided below is the Patentee's failed attempt to address a similar rejection during the prosecution of the '803 Subject Patent, and the substantial new question of patentability raised by this rejection.

i. Patentee's false claim that the application was a <u>Divisional</u> improperly removed this rejection during prosecution

During the prosecution of the '803 Subject Patent, the Examiner issued an obviousness rejection of the claims over Ward et al. and Schach et al.[17] The language in this rejection appears to presuppose that a transgenic mouse expressing an oncogene is known, and that methods of using such mice in

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[16] TPR respectfully notes that a substantial new question of patentability may be based on patents and printed publications previously cited by or to the Office or considered by the Office "if the reference is presented in a new light or a different way that escaped review during earlier examination." (MPEP 2216). This is clearly the case with Ward et al. and Schach et al. as explained in part i. of this section.

[17] Appendix 13, Office Action dated November 2, 1993; page 3.

screening methods would be obvious in view of the screening methods in Ward et al. and Schach et al. In other words, this rejection appears to be combining Ward et al. or Schach et al. with the claims of the '866 Grandparent Patent in a *defacto* nonstatutory obviousness type double patenting rejection as the claims of the '866 Grandparent Patent are to a transgenic mouse expressing an oncogene. The Patentee argued that the '866 Grandparent patent could not be cited as prior art and appeared to tacitly understand that the Examiner may be referencing the *claims* of the '866 Grandparent Patent as they further argued that the '866 Grandparent Patent could not be cited (under 35 U.S.C. 121) as the application was allegedly a divisional application:

> where (***as here***) the divisional application is filed as a result of a restriction requirement in the original case…[T]he Examiner has used Applicants' own teaching concerning the novel and non-obvious oncomice claimed in U.S. Patent No. 4,736,866 (a predecessor to the present case) as though it were prior art, in order to make the claims to methods of using the oncomice appear to be obvious (***emphasis added***).[18]

The Patentee's arguments were ultimately successful as the Examiner withdrew this rejection.

In order for the claims of a patent application to enjoy the protection of 35 U.S.C. 121 several requirements must be satisfied: (i) the USPTO must have issued a Restriction Requirement restricting the claims as claiming a separate invention; and (ii) the patent application must be filed as a divisional application, not a continuation. *See Pfizer Inc. v. Teva Pharmaceuticals USA, Inc*., 518 F3d 1353 (Fed. Cir. 2008) (holding that in order to enjoy the benefits of 35 USC 121, applicants must file restricted claims as a divisional application not a continuation). In this case, TPR respectfully notes that the '803 Subject Patent is not, in fact, a divisional application, and instead was filed as a continuation application as evidenced on the front page of the '803 Subject Patent. It is further noted that the '803 Subject Patent could not have been filed as a divisional application as there was no restriction requirement in the '571 Parent Patent (or even the '866 Grandparent Patent) despite the Patentee's characterization to the Examiner to the contrary. Thus, the '803 Subject Patent fails to satisfy either

[18] Appendix 14: Applicants' February 18, 1994 Response, pages 7-8.

requirement necessary for protection under 25 U.S.C. 121. Moreover, the subject matter claimed in the '803 Subject Patent is virtually identical to subject matter previously prosecuted in the '571 Parent Patent and rejected for double patenting in view of the '866 Grandparent Patent. The purpose of the safe harbor of 23 U.S.C. 121 is to guard against inequities resulting from inconsistent treatment with respect to the separate patentability of claimed subject matter.[19] In the present case, not only was there no restriction requirement in either the '571 Parent Patent or the '866 Grandparent patent, but the history of the '571 Parent Patent reveals that the Patent Office consistently viewed the subject matter ultimately claimed in the '803 Subject Patent to be patentably indistinct from the claims of the '866 Grandparent patent. As such, the claims of the '803 Subject Patent were not entitled to the protection afforded by 35 U.S.C. 121. TPR respectfully submits that the misrepresentation in the '803 Parent Patent file history is relevant to the substantial new question of patentability discussed below as the Patentee never legitimately overcame a rejection of Ward et al. or Schach et al. in view of the transgenic mouse present in the claims of the '866 Grandparent Patent (i.e., it presents an open question of patentability first presented by the Patent Office that has never been properly addressed).

ii. Claim 1 of the '803 Patent is unpatentable under nonstatutory obviousness-type double patenting over Claims 1, 11, and 12 of the '866 Grandparent Patent in Combination with Ward et al. or Schach et al.

Claim 1 of the '803 Subject Patent reads as follows:

> 1. A method of testing a material suspected of being a carcinogen, comprising exposing a transgenic mouse to said material and detecting neoplasms as an indication of carcinogenicity, wherein the germ cells and somatic cells of said mouse contain an activated oncogene sequence introduced into said mouse, or an ancestor of said mouse, at an embryonic stage.

[19] See e.g. *Pfizer Inc. v. Teva Pharmaceuticals USA, Inc.*, 518 F3d 1353 (Fed. Cir. 2008) (noting that applicants ought to be able to "reasonably rely on restriction requirements" and not face double patenting rejections based on previously restricted claims).

Claims 1, 11, and 12 of the '866 Grandparent Patent provide the transgenic mouse recited in Claim 1 of the '803 Subject Patent as these claims provide a transgenic mouse containing an activated oncogene sequence introduced into said mouse or an ancestor of said mouse, at an embryonic stage. Claims 1, 11, and 12 of the '866 Grandparent Patent read as follows:

> 1. A transgenic non-human mammal all of whose germ cells and somatic cells contain a recombinant activated oncogene sequence introduced into said mammal, or an ancestor of said mammal, at an embryonic stage.
>
> 11. The mammal of claim 1, said mammal being a rodent.
>
> 12. The mammal of claim 11, said rodent being a mouse.

In addition to the recited transgenic mouse, Claim 1 of the '803 Subject Patent requires exposing the transgenic mouse to a material suspected of being a carcinogen. Both the Ward et al. and Schach et al. references provide methods of exposing mice to materials suspected of being carcinogens (*See, e.g.*, Abstract of each reference). As such, all the limitations of Claim 1 of the '803 Subject Patent are taught by the combination of Claims 1, 11, and 12 of the '866 Grandparent Patent in combination with either Ward et al. or Schach et al.

TPR respectfully submits that under the guidance of *KSR Int'l Co. v. Teleflex Inc*., Claim 1 of the '803 Subject Patent is unpatentable under obviousness-type double patenting. For example, one basis for finding obviousness, as stated in MPEP § 2141 and 2143, is when the art provides a "simple substitution of one known element for another to obtain predictable results." In this case, substituting the transgenic mouse from the claims of the '866 Grandparent Patent for the non-transgenic mice provided in the suspected carcinogen screening methods of Ward et al. or Schach et al. provides predictable results (e.g., one of skill in the art can screen such animals for the presence of tumors to determine the carcinogenicity, or therapeutic benefits, of particular compounds). As such, TPR respectfully submits that the combination of Claims 1, 11, and 12 of the '866 Grandparent Patent and Ward et al. or Schach et al. raises a substantial new question of patentability under nonstatutory obviousness-type double patenting.

C. SNQ2: Claims 1-3 Are Unpatentable Under the Doctrine of Nonstatutory Obviousness-Type Double Patenting Over Claims 1-12 of the '866 Grandparent Patent

Provided below is a discussion on how the Patentee avoided an obviousness-type double patenting rejection in the '571 Parent Patent prosecution by cancelling claims, as well as a discussion of the substantial new question of patentability raised by such an obviousness-type double patenting rejection as applied to the '803 Subject Patent claims.

i. The Patentee's Cancelling of Claims in the '571 Parent Patent Removed this Rejection

During the prosecution of the '571 Parent Patent, Examiner Tanenholtz rejected Claims 13, 18, and 19 on the grounds of nonstatutory obviousness-type double patenting in view of Claims 1-12 of the '866 Grandparent Patent. In particular, Examiner Tanenholtz wrote:

> Claims 13, 18 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claims 1-12 of U.S. patent no. 4,736,866. Although the conflicting claims are not identical, they are not patentably distinct from each other because the testing procedure of claims 13, 18 and 19 is the obvious use of the claimed mammal. (*emphasis added*).[20]

Claims 13, 18, and 19 correspond nearly identically to issued Claims 1-3 of the subject '803 Subject Patent (compare '803 Claims at Appendix 1 with the '571 filed claims at Appendix 8). In response to this rejection in the '571 Parent Patent prosecution, the Patentee filed the terminal disclaimer discussed above, thereby mooting this rejection, and later cancelled the claims to obviate an enablement rejection. However, claims of meaningful identical scope were re-presented in the subject '803 Subject Patent but the highly relevant art was not used as a basis for rejection. As discussed below, this art should have been applied in a rejection. Regardless, in view of the current law of obviousness, the claims should be rejected in Reexamination.

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[20] Appendix 15: Office Action in '571 patent prosecution dated November 14, 1985, page 2).

ii. Claims 1-3 Are Unpatentable Under the Doctrine of Nonstatutory Obviousness-Type Double Patenting Over Claims 1-12 of the '866 Grandparent Patent

In agreement with the rejection by Examiner Tanenholtz in the '571 Parent Patent prosecution, TPR respectfully submits that Claims 1-3 of the '803 Subject Patent are unpatentable under the doctrine of nonstatutory obviousness-type double patenting in view of Claims 1-12 (or at least Claims 1, 11, and 12) of the '866 Grandparent Patent. As asserted by Examiner Tanenholtz, TPR submits that such a rejection is proper because the testing procedure in Claims 1-3 of the '803 Subject Patent "is the obvious use of the claimed mammal" in the '866 Grandparent Patent claims. Stated another way, one of skill in the art would necessarily understand the *purpose* for which the transgenic mice in the '866 Grandparent Patent claims were created was for screening carcinogens and protective compounds - thereby rendering the '803 Subject Patent claims not patentably distinct. As such, TPR respectfully submits that this raises a substantial new question of patentability under nonstatutory obviousness-type double patenting.

D. SNQ3: Claims 2-3 Are Unpatentable Under Nonstatutory Obviousness-Type Double Patenting Over Claims 1, 11, and 12 of the '866 Grandparent Patent in View of the Proctor Patent

The Proctor patent was published on November 23, 1982, which is more than one year before the earliest filing date (June 22, 1984) of the '803 Subject Patent, and therefore qualifies as prior art under 35 U.S.C. §§ 102(b) and 103(a). The combination of Claims 1, 11, and 12 of the '866 Grandparent Patent and the Proctor patent raises a substantial new question of patentability as described below.

Claims 2-3 of the '803 Subject Patent read as follows:

> 2. A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising
> (1) providing a first and a second transgenic mouse, the germ cells and somatic cells of which contain an activated oncogene sequence introduced into said mice, or an ancestor of said mice, at an embryonic stage,
> (2) treating said first mouse with said material, and

(3) detecting, as an indication of said protection, a reduced incidence of development of neoplasms in said first mouse, compared to the incidence in said second mouse, which is not so treated.

3. The method of claim 1[21], further comprising exposing said first and second mice to a carcinogen prior to, after, or simultaneously with treating said first mouse with said material.

Claims 1, 11, and 12 of the '866 Grandparent Patent provide the transgenic mice recited in Claims 2 and 3 of the '803 Subject Patent as these claims provide transgenic mice containing an activated oncogene sequence introduced into said mouse or an ancestor of said mouse, at embryonic state. Claims 1, 11, and 12 of the '866 Grandparent Patent read as follows:

1. A transgenic non-human mammal all of whose germ cells and somatic cells contain a recombinant activated oncogene sequence introduced into said mammal, or an ancestor of said mammal, at an embryonic stage.

11. The mammal of claim 1, said mammal being a rodent.

12. The mammal of claim 11, said rodent being a mouse.

In addition to the recited transgenic mouse, Claim 2 of the '803 Subject Patent requires treating a first transgenic mouse with a material suspected of conferring protection against the development of neoplasms (i.e., a candidate anti-tumor agent) and detecting a reduced incidence of development of neoplasms compared to a second untreated mouse. Claim 3 of the '803 Subject Patent further requires exposing the mice to a carcinogen. The Proctor patent provides methods of treating a first mouse with a candidate anti-tumor agent and comparing to a second control mouse not treated with the anti-tumor agent, wherein both the first and second mice are administered radiolabelled tumor cells (i.e., a carcinogen) (see, e.g., col. 5, line 25 - col. 6, line 7). The teaching of the Proctor patent is well summarized in Claim 1 of this patent:

[21] While Claim 3 is indefinite, it is noted that, for purposes of this analysis, it has been assumed that Claim 3 is dependent on Claim 2, despite the fact that it references Claim 1, since only Claim 2 has first and second mice as recited in Claim 3.

1. A method for determining the anti-tumor activity of an agent of the reticulo-endothelial stimulant class comprising the sequential steps of:

(1) administering predetermined doses of an anti-tumor agent of the reticulo-endothelial stimulant class to a rodent, by a suitable route of administration;

(2) at between 2 and 60 days, thereafter, administering a predetermined quantity of radiolabelled tumor cells, radiolabelled with a DNA label, to said rodent;

(3) allowing the administered radiolabelled tumor cells to build up in the lung and subsequently allowing at least about 50% of said cells to be lost from the lung of said rodent;

(4) isolating the lung tissue from said rodent and measuring the radioactivity emanating from the remaining radiolabelled tumor cells in said isolated piece of tissue; and thereafter

(5) calculating the increase in loss of said radioactivity from said isolated piece of lung tissue of a predetermined size from animals treated with said anti-tumor agent of the reticulo-endothelial stimulant class, compared with the loss of radioactivity from a piece of lung tissue of substantially the same predetermined size isolated from rodents receiving no or a placebo treatment, the increase representing an index of the magnitude of the anti-tumor effect observed.

As such, all the limitations of Claims 2-3 of the '803 Subject Patent are taught by the combination of Claims 1, 11, and 12 of the '866 Grandparent Patent in combination with the Proctor patent.

TPR respectfully submits that under the guidance of *KSR Int'l Co. v. Teleflex Inc*., Claims 2 and 3 of the subject '803 Subject Patent are unpatentable under obviousness-type double patenting. For example, one basis for finding obviousness, as stated in MPEP § 2141 and 2143, is when the art provides a "simple substitution of one known element for another to obtain predictable results." In this case, substituting the transgenic mouse from the claims of the '866 Grandparent Patent for the non-transgenic mice (tumor cell treated mice) provided in the anti-tumor agent screening methods of the Proctor patent provides predictable results (e.g., one of skill in the art can screen such animals for the presence of tumors to determine the anti-tumor properties of particular compounds). As such, TPR respectfully submits that the combination of Claims 1, 11, and 12 of the '866 Grandparent Patent and

the Proctor patent raises a substantial new question of patentability under nonstatutory obviousness-type double patenting.

E. SNQ4: Claims 1-3 Are Unpatentable Under 35 U.S.C. 103(a) in View of Schwab

Schwab et al. was published in July of 1982, which is more than one year before the earliest filing date (June 22, 1984) of the '803 patent, and therefore qualifies as prior art under 35 U.S.C. §§ 102(b) and 103(a).

During the prosecution of both the '866 Grandparent Patent and '571 Parent Patent, claims corresponding to those that issued in the '803 Subject Patent were rejected as obvious over Schwab et al. by Examiner Tanenholtz.[22] The text of these two rejections is provided below:

> Claims 13 and 15-19 are rejected under 35 U.S.C. 103 as being unpatentable over Schwab et al who disclose the claimed process differing essentially in using a different animal. However, it is considered that the claimed process is unpatentable over those references in view of *In re Durden, Jr.* et al 226 USPQ 362 which held that;
>
> > "A new process may still be obvious, even when considered "as a whole", notwithstanding the specific starting material or resulting products, or both is not found in the prior art". (Rejection '866 grandparent; Appendix 16).and
>
> Claims 13, 18 and 19 are rejected under 35 U.S.C. 103 as being unpatentable over Schwab et al who teach using oncogene containing multicellular animals as a tool for monitoring carcingoenes. In view of the 35 USC 112 deficiencies supra the claims are not considered to patentably distinguish from Schwab et al. (Rejection in '571 parent prosecution; Appendix 15)

The Patentee avoided these rejections each time by <u>cancelling</u> these corresponding claims. When these same claims were re-presented in the '803 subject patent prosecution, this art was not applied in a rejection. As such, this necessarily raises a new substantial question of patentability as the Patentee has never addressed this rejection.

As indicated by Examiner Tanenholtz in the '866 Grandparent Patent and '571 Parent Patents, the Schwab et al. reference teaches oncogene containing multicellular animals as a tool for monitoring

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[22] See Appendix 16: Non-Final Office Action dated November 3, 1986 in the '866 Grandparent Patent, page 5; and Appendix 15: the Final Office Action dated July 31, 1987, in the '571 Parent Patent, page 4.

carcinogens. In particular, the Schwab et al. reference employed freshwater fish called *Xiphophorus*. One particularly relevant passage from Schwab et al. states:

> As it is, construction of genotypes by selective breeding carrying several oncogenes conferring hypersensitivity should be a powerful tool for creating suitable *test organisms* [not just fish] and at the same time may provide further clues towards an understanding of cancer genes in malignancy. (emphasis added, Schwab et al., page 227).

TPR submit that Examiner Tanenholtz's rejection was proper and is even more appropriate now in view of the Supreme Court holding in *KSR Int'l Co. v. Teleflex Inc.* (see discussion above). As such, TPR respectfully submits the '803 Subject Patent claims should be rejected as obvious over Schwab et al. as this reference raises a substantial new question of patentability.

F. SNQ5: Claims 2-3 Are Unpatentable Under 35 U.S.C. 103(a) Over Jaenisch et al. in View of the Proctor patent

Jaenisch et al. was published in 1974, which is more than one year before the earliest filing date (June 22, 1984) of the '803 Subject Patent, and therefore qualifies as prior art under 35 U.S.C. §§ 102(b) and 103(a). As indicated above, the Proctor patent published in 1982, and therefore also qualifies as prior art under 35 U.S.C. §§ 102(b) and 103(a).

The inventors of the '803 Subject Patent were not the first to generate transgenic mice. The Jaenisch laboratory is generally credited with this distinction. Indeed, numerous groups had generated transgenic mice prior to the '803 Subject Patent.[23] Such animal models were well known to be useful in compound screening. This is exemplified by the combination of Jaenisch et al. and the Proctor patent.

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[23] See, e.g., Gordon and Ruddle, Prog. Cin. Biol. Res. 85 Ptb:111-24 (1982); Palmiter et al., Cell, 29(2):701-710 (1982); Palmiter et al., Nature, 300 (5893):611-5 (1982); Gordon and Ruddle, Methods Enz., 101:411-31 (1983); Lacy and Costantini, Prog. Clin. Biol., Res, 134:13-25 (1983); McKnight et al., Cell 34(2):335-41 (1983); Lacy et al., Cell, 34(2):343-58 (1983); Gordon, J. Exp. Zool., 228(2):313-24 (1983); Palmiter et al., Science, 222(4625):809-14 (1983); and Brinster et al., Nature, 306 (5941):332-6 (1983).

i. Claims of the '803 Patent Do Not Require that it is the "activated oncogene sequence" that necessarily causes neoplasms in the mice

One important claim interpretation issue to address prior to discussing the merits of an obviousness rejection over Jaenisch et al. and the Proctor patent relates to the fact that the plain language of the '803 Subject Patent claims does not require that it be the "activated oncogene sequence" that necessarily causes neoplasms in the mice. An examination of independent Claims 1 and 2 reveals that the recited mice must necessarily have an "activated oncogene sequence," but nowhere in these claims does it recite that this activated oncogene necessarily *causes* the neoplasms that are detected. Instead, the plain language of the claim (e.g., using "comprising") allows not only the activated oncogene sequence to cause the neoplasms, but also allows for anything else to be the cause of the neoplasms - such as naturally occurring neoplasms or exposure to carcinogens. This interpretation of Claims 1 and 2 is confirmed by Claim 3 which recites:

> 3. The method of claim 1 [Claim 2][24], further comprising exposing said first and second mice to a carcinogen prior to, after, or simultaneously with treating said first mouse with said material.

Claim 3 makes it explicit that other agents may be used (i.e., carcinogens) to cause neoplasms in the mice, and therefore, the "activated oncogene sequence" is not necessarily what causes the mice to have neoplasms.

It is further noted that the definition of an "activated oncogene sequence" provided in the '803 Subject Patent specification makes it clear that such sequences do not necessarily cause neoplasms. In particular, the '803 Subject Patent states:

> An activated oncogene sequence, as the term is used herein, means an oncogene which, when incorporated into the genome of the animal, increases the *probability* of the development of neoplasms (particularly malignant tumors) in the animal. (*emphasis added,* col. 1, lines 40-45).

This definition of "activated oncogene sequence" makes it clear that such sequences only increase the probability of neoplasms occurring without necessarily causing neoplasms. Again, this supports the plain language of the claims where the "activated oncogene sequence" is not necessarily (i.e., in all embodiments) what causes the mice to have neoplasms.

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[24] See *supra* note 22.

ii. Claims of the '803 Patent Do Not Require that every cell in the animals carry the transgene

As interpreted in their broadest form, the claims of the '803 Subject Patent do not require that every somatic or germ cell in the animal carry the transgene. Thus, any transgenic animal that contains some cells harboring transgenes in somatic and germ cells is relevant prior art. This is in contrast to the '866 Grandparent Patent that claimed animals where all of the cells are transgenic. Thus, while the claimed Grandparent Patent animal is an example of an animal as claimed in the '803 Subject Patent and serves as double patenting prior art, a much wider range of transgenic animals provide suitable prior art against the claims of the '803 Subject Patent, including those listed above.

iii. Claims 2-3 Are Unpatentable Under 35 U.S.C. 103(a) Over Jaenisch et al. in View of the Proctor patent

Claims 2 and 3 of the subject '803 Subject Patent are unpatentable under 35 U.S.C. 103(a) over Jaenisch et al. in view of the Proctor patent. Claims 2-3 of the subject '803 patent read as follows:

> 2. A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising
> (1) providing a first and a second transgenic mouse, the germ cells and somatic cells of which contain an activated oncogene sequence introduced into said mice, or an ancestor of said mice, at an embryonic stage,
> (2) treating said first mouse with said material, and
> (3) detecting, as an indication of said protection, a reduced incidence of development of neoplasms in said first mouse, compared to the incidence in said second mouse, which is not so treated.
>
> 3. The method of claim 1, further comprising exposing said first and second mice to a carcinogen prior to, after, or simultaneously with treating said first mouse with said material.

The Jaenisch et al. reference provides the transgenic mice recited in Claims 2 and 3 of the '803 Subject Patent as this reference provides transgenic mice containing an activated oncogene sequence introduced into said mouse or an ancestor of said mouse, at embryonic state. In particular, Jaenisch et al. provides transgenic mice that contain SV40 viral DNA in their germ and somatic cells. SV40 viral DNA qualifies as an "activated oncogene sequence," according to the definition in the '803 Subject

Patent specification, as SV40 is known to be oncogenic (*see*, e.g., wikipedia entry: http://en.wikipedia.org /wiki/SV40; and Smith, J. Cell. Biochem., 26(2):89-93, 1984). Moreover, while the Jaensich et al. reference acknowledges that no apparent tumors were generated by 1 year of age, as discussed above, the '803 Subject Patent claims do not require that the activated oncogene sequence causes tumors. As such, the Jaenisch et al. reference meets all of the requirements of the transgenic mice in Claims 2 and 3 of the '803 Subject Patent.

In addition to the recited transgenic mouse, Claim 2 of the '803 Subject Patent requires treating a first transgenic mouse with a material suspected of conferring protection against the development of neoplasms (i.e., a candidate anti-tumor agent) and detecting a reduced incidence of development of neoplasms compared to a second untreated mouse. Claim 3 of the '803 Subject Patent further requires exposing the mice to a carcinogen. The Proctor patent provide methods of treating a first mouse with a candidate anti-tumor agent and comparing to a second control mouse not treated with the anti-tumor agent, wherein both the first and second mice are administered radiolabelled tumor cells (i.e., a carcinogen) (*see*, e.g., col. 5, line 25 - col. 6, line 7). As such, all the limitations of Claims 2-3 of the '803 Subject Patent are taught by the combination of Jaenisch et al. in combination with the Proctor patent.

TPR respectfully submits that under the guidance of *KSR Int'l Co. v. Teleflex Inc*., Claims 2 and 3 of the '803 Subject Patent are unpatentable as obvious in view of Jaenisch et al. and the Proctor patent. For example, one basis for finding obviousness, as stated in MPEP § 2141 and 2143, is when the art provides a "simple substitution of one known element for another to obtain predictable results." In this case, substituting the transgenic mouse from the Jaenisch et al. reference into the methods of the Proctor patent that employ non-transgenic mice provides predictable results (e.g., one of skill in the art can screen such animals for the presence of tumors to determine the anti-tumor properties of particular compounds). As such, TPR respectfully submits that the combination of Jaenisch et al. and the Proctor patent raises a substantial new question of patentability under 35 U.S.C. 103(a).

G. SNQ6: Claim 1 Is Unpatentable Under 35 U.S.C. 103(a) Over Jaenisch et al. in View of Ward et al. or Schach et al.

Claim 1 of the '803 Subject Patent is unpatentable under 35 U.S.C. 103(a) over Jaenisch et al. in view of Ward et al. or Schach et al. Claim 1 of the '803 Subject Patent reads as follows:

> 1. A method of testing a material suspected of being a carcinogen, comprising exposing a transgenic mouse to said material and detecting neoplasms as an indication of carcinogenicity, wherein the germ cells and somatic cells of said mouse contain an activated oncogene sequence introduced into said mouse, or an ancestor of said mouse, at an embryonic stage.

The Jaenisch et al. reference provides the transgenic mouse recited in Claim 1 of the '803 Subject Patent as this reference provides transgenic mice containing an activated oncogene sequence introduced into said mouse or an ancestor of said mouse, at embryonic state. In particular, Jaenisch et al. provides transgenic mice that contain SV40 viral DNA in their germ and somatic cells. SV40 viral DNA qualifies as an "activated oncogene sequence," as discussed above. As such, the Jaenisch et al. reference meets all of the requirements of the transgenic mouse in Claim 1 of the '803 Subject Patent.

In addition to the recited transgenic mouse, Claim 1 of the '803 Subject Patent requires exposing the transgenic mouse to a material suspected of being a carcinogen. Both the Ward et al. and Schach et al. references provide methods of exposing mice to materials suspected of being carcinogens (*See, e.g.*, Abstract of each reference). As such, all the limitations of Claim 1 of the '803 Subject Patent are taught by the combination of Jaenisch et al. in combination with either Ward et al. or Schach et al.

TPR respectfully submits that under the guidance of *KSR Int'l Co. v. Teleflex Inc.*, Claim 1 of the '803 Subject Patent is unpatentable as being obvious. For example, one basis for finding obviousness, as stated in MPEP § 2141 and 2143, is when the art provides a "simple substitution of one known element for another to obtain predictable results." In this case, substituting the transgenic mouse from the Jaenisch et al. reference for the non-transgenic mice provided in the suspected carcinogen screening methods of Ward et al. or Schach et al. provides predictable results (e.g., one of skill in the art can screen such transgenic mice for the presence of tumors to determine the carcinogenicity of particular compounds). As such, TPR respectfully requests that the combination of Jaenisch and Ward et al. or Schach et al. raises a substantial new question of patentability under 35 U.S.C. 103(a).

CONCLUSION

In view of the foregoing, TPR respectfully:

A. Submits that substantial new questions of patentability exist as to all claims of the '803 Subject Patent and requests that the Office identify each claim unpatentable for the reasons set forth above; and

B. Requests that the Patent Office issue a statement stating that the ‘803 Subject Patent expired July 12, 2005 by way of a terminal disclaimer.

Respectfully submitted,

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